National Institute on Alcohol Abuse and Alcoholism

RESEARCH
Monograph-5

Evaluation of the Alcoholic: Implications for Research, Theory, and Treatment

EPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

National Institute on Alcohol Abuse and Alcoholism

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Research Monograph No. 5

EVALUATION OF THE ALCOHOLIC: IMPLICATIONS FOR RESEARCH, THEORY, AND TREATMENT

Proceedings of a Conference
October 12-13, 1979
Farmington, Connecticut

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National Research Centers Branch, NIAAA

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This publication is the product of a research workshop on evaluation of the alcoholic in terms of the implications for research, theory, and treatment held in **Farmington**, Conn., Oct. 12-13, 1979, under grant P50 AA03510 awarded **by the National Institute on Alcohol Abuse and Alcoholism** to the University of Connecticut Health Center. The presentations herein are those of the listed authors and may not necessarily reflect the opinions, official policy, or position of the National Institute on Alcohol Abuse and Alcoholism; the Alcohol, Drug Abuse, and Mental Health Administration; the Public Health Service; or the U.S. Department of Health and Human Services.

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Library of Congress Catalog Card Number: 80-600132

DHHS Publication No. (ADM) 81-1033
Printed 1981

For sale by the Superintendent of Documents, U.S. Goverment Printing Office,
Washington, D.C. 20402

Foreword

This volume is another in the National Institute on Alcohol Abuse and Alcoholism's series of research monographs. The series sets forth current information on a number of topics relevant to alcohol abuse and alcoholism as reported through workshops in research, prevention, and treatment, as well as through state-of-the-art reviews on selected subjects.

The NIAAA has had a longstanding commitment to broadly disseminate information from researcher to researcher in order to promote new advances in our knowledge about alcoholism. Of equal importance, however, is the NIAAA commitment to transfer newly developed information to persons entrusted with the care and treatment of alcoholic patients and their families. It is our hope that this monograph series enhances the prospects that these commitments will be fulfilled.

John R. DeLuca
Director
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Preface

This monograph reports the proceedings of a national symposium held in October 1979 and cosponsored by the University of Connecticut Alcohol Research Center and the NIAAA. The Alcohol Research Center is one of nine National Alcohol Research Centers funded by the NIAAA. Each Center focuses on a central theme of importance to the study of alcoholism, ranging from the neurophysiological effects of alcohol consumption to how social policy and law influence the production, distribution, and consumption of alcohol. In addition to their primary mission of developing new knowledge through original research in their chosen areas within the field of alcoholism, the Centers are responsible for disseminating that knowledge broadly across scientific and lay communities. In this connection, the Centers have joined the NIAAA in organizing and holding workshops and conferences on topics close to their specialty areas. The proceedings in this volume represent one of these collaborative activities.

The purpose of the Connecticut symposium was to address the general notion of differential assessment as it applies to persons diagnosed as alcoholic. The medical literature is replete with descriptive categories, classification schemes, and typological groupings of alcoholic persons. Unfortunately, these efforts at differentiation show little consistency in terms of theoretical assumptions, empirical bases, and treatment implications. The papers presented at the symposium and printed here examine these issues and should serve to identify promising developments in clinical as well as research program activities.

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Introduction

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It is a generally accepted truism that when a variety of treatments exist for a given disorder, none of these treatments is associated with a high order of success. A corollary assumption often made is that the success rate of any given treatment would be significantly enhanced by greater attention to the patient-selection process. Historically, alcohol rehabilitation has been characterized by widely differing approaches to treatment which have too often been based on differences in ideology rather than differences in patient characteristics (Pattison 1974). For the most part, attempts to differentiate specific treatment-responsive subpopulations have depended on social and psychological variables and on differences in drinking patterns (Towle 1975). Paradoxically, while there has been an increasing interest in treatment-relevant psychiatric diagnoses in the major psychoses and affective disorders, based in part on family pedigree and biological variables (Gershon et al. 1976; Wyatt and Gillin 1976; Stabenau 1977), there has not been much work on this approach in the field of alcoholism. One major reason for the interest in treatment-relevant typologies in psychiatry has been the introduction of lithium carbonate in the treatment and prophylaxis of bipolar illness (Gershon and Shopsin 1973). The still imperfect criteria for the diagnosis of bipolar affective disorder are based on symptomatology, natural history, and family pedigree data (Winokur et al. 1970).

In contrast to the literature on affective disorders, there have been few systematic attempts to differentiate subpopulations of alcoholics, although a critical reading of the treatment literature reveals widespread disenchantment with the homogenization of the alcoholic patient population by the treatment community (Pattison 1976; Pokorny et al. 1968; Trice et al. 1969; Wanberg and Knapp 1970). Most agree that typological differentiation would be useful only to the extent that it would suggest differential response to treatment, differential treatment assignment, or intrinsic differences in prognosis. The suggestion of primary versus reactive alcoholism (Ryback 1974) suggests the importance of psychopathology and stress in the etiology of some forms of alcoholism.

There appears to be an inverse relationship between the amount of psychopathology associated with alcoholism in a given society or subculture and the tolerance of that society for drinking or for heavy drinking (Robins 1977). For example, residents of a fundamentalist abstinent environment who use alcohol tend to be deviant and tend to go on to develop alcoholism. In contrast, male heavy drinkers in this society tend to have much less psychopathology than females who drink the same amount. Thus, typologies of alcoholics based on psychopathology may be culturally specific and may suggest a different prognostic course within the relative limits of the culture. One might be able to describe a typology of alcoholics based on psychopathology in one geographic region of the United States, but this typology might not hold up elsewhere. Moreover, individual alcoholics manifest more psychopathology while intoxicated and during the period of immediate withdrawal from alcohol. Secondary depression is particularly noticeable during both of these periods. This secondary psychopathology may also have prognostic or therapeutic significance.

The notion of a genetic pool of primary alcoholics comes out of the work of Winokur et al. (1970), Goodwin (1971), and Schuckit et al. (1976). The genetic factor may not apply to all alcoholics (Mendelson 1975), and family pedigree issues may therefore be important in suggesting a typology. As Theodore Reich points out later in this volume, genetic diathesis is not a static idea, but suggests the importance of an environmental trigger essential to gene expression. There is a missing link between the obvious familial pattern of alcoholism and the idea of a predisposing genetic factor. It is this genetic factor which has not been identified.

The group at the Carrier Clinic has suggested that minimal brain dysfunction serves as a predisposing factor to alcoholism (Mendelson 1975). The evidence for this point of view is spelled out by Dr. Ralph Tarter later in this volume. Brain dysfunction also is a consequence of alcohol use. Central nervous system impairments and other biological consequences of alcohol use also may lead to differentiation within the alcoholic population. Not all alcoholics, for example, develop central nervous system impairment or liver pathology. Clearly, associated neurological, hepatic, or other medical pathology will affect prognosis and response to treatment; indeed, they will affect mortality. Thus, the consequences of alcohol use can be used to differentiate meaningful typologies.

The earliest effects at differentiation within the alcoholic population were of course the categories based on patterns of alcohol use described by Jellinek (1960). These are important, not only in establishing the diagnosis of alcoholism based on actual quantities and patterns of alcohol consumed, but also in identifying a subgroup of alcoholics who manifest "loss of control drinking." Careful assessment of patterns of use, a history of loss of control, and actual observations of alcoholics under conditions of access to alcohol could serve to differentiate other typologies.

The importance of the concept that all alcoholics are not alike should ultimately mean that we may be able to improve our treatments and make them more specific for individual patients. This is the essence and purpose of diagnosis. We are at a very early stage in this process in the study of alcoholism. This book represents a state-of-the-art review of the differential assessment of the alcoholic (including problems of quantification, assessment of psychopathology, the implications of alcoholic pedigree, the behavioral assessment of the alcoholic, and an overview of the varieties of negative outcome observed in patients) which may have implications for research, theory, and treatment. The volume also includes a series of papers on the assessment of treatment impact, including studies of long-term outcome in large samples of subjects. The papers were presented at a national meeting sponsored by the University of Connecticut Alcohol Research Center and the NIAAA.

The Alcohol Research Center at the University of Connecticut is one of nine national research centers the NIAAA funds to advance the scientific understanding of alcoholism. Researchers at the University come from a variety of disciplines and are collaborating in studies of alcoholic subtypes, treatment effectiveness, and alcoholic psychopathology, as well as of the biomedical, genetic, behavioral, and cross-national aspects of alcoholism. Senior scientists at the University of Connecticut served as moderators and discussants at the meeting in October 1979 and as editors of this volume. Faculty participating included:

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EDITOR'S COMMENT: EVALUATING THE EVALUATION PROCESS*

Thomas F. Babor

Students of alcohol problems have disagreed about the meaning of alcoholism since the term "alcoholismus" was invented in 1849 by Magnus Huss. While disagreement seems to be as intense as ever, the papers collected in this volume reveal that considerable progress has been made in establishing the ground rules for a resolution of the dispute. The papers were presented at a research conference organized by the University of Connecticut Alcohol Research Center and sponsored by the National Institute on Alcohol Abuse and Alcoholism.

The conference theme, "Evaluation of the Alcoholic," was chosen to address the general notion of differential assessment as it applies to persons already diagnosed as alcoholic. Evaluation implies the application of empirical methods to the study of alcohol dependence and its related physical, mental, and social disabilities. One assumption guiding the selection of this theme was that advances in clinical treatment and prevention have traditionally followed advances in evaluation. By way of introducing the present contributions, it would therefore be instructive to review briefly the historical evolution of alcohol studies in America.

Progress was first made when the concept of drunkenness was "medicalized" in the early 19th century, initially in the form of a moral-physical condition called "intemperance," and later as a physical and psychological disease we have come to label "alcoholism." In colonial times the drunkard was viewed as a sinner and drunkenness was considered a moral vice, at least by the educated Protestant clergy from whose writings most accounts are drawn (Levine 1978). Because intoxication was assumed to result from the individual's free choice, the drunkard, not society or the bottle, was considered responsible for the resulting condition. After the

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* Writing of this paper was supported in part by a Research Scientist Development Award (No. 5 KO1 AA 00025-03) from the National Institute on Alcohol Abuse and Alcoholism.

American Revolution this traditional "free will" or moral vice position was rivaled, if not supplanted, by a radically different "disease" concept. That concept exculpated the drinker from moral responsibility by attributing causality to either the agent (initially spirits), or the condition (intemperance—a progressive, addictive disease), or both. Articulated most clearly in the medical writings of physicians such as Benjamin Rush (1790) and Samuel Woodward (1838), this early physical disease model of alcoholism became a dominant feature of temperance ideology. It also provided the intellectual foundation of 20th century disease conceptions (Levine 1978). These conceptions have since assumed an additional dimension favoring psychological causes, beginning with the "psychological disease theories" advanced in the late 19th century (Jaffe 1978).

It is important to note that the present disease concept evolved out of a series of ideological conflicts among members of the clergy, temperance advocates, reformed alcoholics, mental health professionals, and, most important, physicians. Traditionally, the alcoholic has been evaluated using the tools available, be they moral standards, social norms, physical examinations, psychological tests, or biochemical analyses. And each time a new technology was added to the armamentarium of evaluation, advances were made in our understanding of alcoholism as a multidimensional disorder having multiple etiologies.

Although both the medical and social sciences made tremendous advances during the first half of the 20th century, alcohol studies seem to have languished while the Nation experimented with a political solution. Then, in the 1950s, E.M. Jellinek rediscovered and redefined the disease concept in a way that gave inspiration to clinicians and researchers alike. But in his now classic *The Disease Concept of Alcoholism* (1960), Jellinek planted the seeds of a revisionist spirit which was to be the bane of dogmatists and purists during the 1970s.

Written as they were at the very end of the 1970s, the papers in this volume are fascinating in terms of what they reveal about the decade in alcohol studies, a decade that was perhaps one of the most exciting and controversial since total abstinence was first advanced as the only cure for alcoholism (Woodward 1838). That conceptual confusion, methodological mediocrity, and ideological chauvinism currently pervade the field is evident from the iconoclastic posture many researchers are forced to assume in posing their research questions. Can alcoholism be considered as a unitary disease entity? Are the consequences of excessive alcohol consumption common enough among all alcoholics to permit unequivocal diagnosis? Can drinking behavior and its consequences be measured reliably and accurately? Are persons diagnosed as alcoholics distinguishable into homogeneous subtypes? And, finally, does treatment work? Recurring time and again throughout these pages, these questions say a great deal about what now preoccupies researchers and clinicians in the field. This preoccupation generally reduces to two major themes. The first deals with the issue of diagnosis, definition, and conceptualization; the second with the multivariate nature of alcoholism and the need to differentiate among subgroups of alcoholics.

Does alcoholism exist as a unitary disease entity? Directly or indirectly, more than half of the papers in this collection touch upon the topics of definition, diagnosis, or nosology. To ponder the nature and meaning of alcoholism is no mere academic exercise. Our concepts and definitions represent important preconceptions about our perception of reality. They influence our selection of data and are often maintained long after the evidence fails to conform to them. Disparagement of the unitary disease concept may seem like sacrilege to some. To others it may be tantamount to setting the torch to the proverbial strawman. But like Milton's "stubborn unlaid ghost/ That breaks his magic chains at curfew time," its spirit haunts all current thinking about alcoholism.

In the opening papers in section I, Mansell Pattison and Alan Marlatt focus on the major dilemma: Does the construct we have come to call alcoholism lend itself to definition by formal criteria? Does our definition permit easy differentiation between alcoholics and nonalcoholics? What appears first as an almost frivolous semantic game shows itself upon closer inspection to have much deeper implications. Yes, for social, political, and even humanitarian reasons it might be useful to argue that alcoholism is a unitary disease having a prescribed etiology from physical causes which produce a consistent pattern of signs and symptoms. Such a concept removes blame from the patient, responsibility from society, and gives everyone a reassuring explanation for the patient's behavior and illness. But from the scientific and therapeutic points of view, it may be more fruitful to argue that the unitary disease concept, and its attendant binary classification rule, is fraught with difficulties and disadvantages. It is not consistent with the diversity of symptomatology found among persons labeled alcoholic, it restricts our attention to only the medical reality of alcoholism, and it fails to account for the variety of ways in which alcohol-related disabilities are manifested.

Central to our efforts to develop a useful definition is the need to specify operational criteria for alcohol dependence and alcohol-related damage. As discussed in papers by Lee Robins and Peter Nathan, considerable progress has been made in developing a more dimensional set of operational criteria. If at one time a major goal of the therapeutic process was to have the patient admit "I am an alcoholic," it may now be time to elaborate the confession to "I am an alcoholic who is dependent on alcohol to a certain (slight, moderate, or severe) degree, who is disabled to a certain degree in certain areas of (physical, psychological, or social) functioning, and whose problem is primarily attributable to certain (physical, psychological, or environmentally induced) vulnerabilities." There is no question among these authors that there are real alcoholics. The problem, and the paradox, is that there seems not to be any one specific entity conforming to our current notions of alcoholism. Rather, there appears to be a whole group of related syndromes whose only common characteristics are drinking, dependence, and damage.

This brings us to the second major theme reiterated throughout these papers: the multivariate nature of alcoholism and the need to differentiate among alcoholic subtypes. The medical literature is replete with descriptive categories, classification schemes, and typological groupings of alcoholics. There are gammas and deltas, primaries and secondaries, reactives and essentials, even precipitated and "screwed up" alcoholics (Wilson 1977). Unfortunately, these efforts at differentiation show little consistency in terms of theoretical assumptions, empirical bases, or treatment implications. Part of the difficulty is suggested in the paper by Raymond Costello. Researchers as well as theorists have not specified their levels of analysis with sufficient rigor, even within the relatively circumscribed area of personality assessment. Thus it is not surprising that the search for consistent subtypes has been impeded by both conceptual and methodological problems. Methodology may now be less of an impediment because of the revolutionary advances in computer technology, differential assessment, and multivariate statistics. But the ultimate programer of our high-powered technology still remains the human cortex. Only the theorist and clinician can decide which variables to include in the analysis, and how the resulting relationships should be interpreted. Viewed in their entirety, the papers in this collection suggest the importance of distinguishing among at least five levels of analysis in any future taxonomy of alcoholics.

First, alcoholics should be differentiated separately on the basis of etiology and antecedent conditions. In section III, Donald Goodwin documents the importance of family history, Theodore Reich suggests how genetics may interact with environment, and Michie Hesselbrock and Ralph Tarter implicate various psychopathologies. In other papers by Remi Cadoret and Nancy Mello, psychological states and state changes are advanced as possible etiological factors. Finally, Peter Nathan and Arnold Ludwig emphasize learning history and environmental conditions. With such a diversity of origins and causes in the backgrounds of alcoholics, it is not surprising that they should differ in other respects as well.

A second level of analysis is drinking pattern. This refers to the quantity, frequency, and variability of alcohol consumption. Drinking style may differentiate male from female alcoholics, and primary from secondary alcoholics. George Vaillant and David Armor both suggest that following relapse alcoholics differ greatly in their relative ability to control their drinking. A question that has not been answered with any degree of satisfaction is whether different drinking patterns result in different types of consequences.

Yet another level of analysis suggested in these papers is the syndrome of alcohol dependence. There is a growing consensus that dependence is the most obvious organizing principle upon which to base an operational definition of alcoholism. While there are practical problems involved in the measurement of tolerance, withdrawal, and other dependence symptoms, the findings of Armor and Vaillant relating to prognosis suggest that alcoholics can and should be differentiated on this variable. Inasmuch as the phenomenon of loss of control over drinking falls within the domain of dependence, as suggested in the paper by Arnold Ludwig, alcohol dependence falls within the domain of physical disease.

A fourth level of analysis discussed in these papers is that of alcohol-related disabilities. Alcoholics differ not only in terms of antecedents, drinking patterns, and dependence; they also differ markedly in terms of physical deterioration. Why do only a minority of patients develop alcoholic cirrhosis and other ethanol-induced organ pathologies? Reviews by Robert Scheig, Charles Lieber, and Michael Eckardt suggest how physical vulnerability, age, sex, organ weakness, nutrition, and other factors may interact with ethanol to potentiate the risk of medical illness. In this respect we might include the elusive research for the golden ruler with which to measure preclinical signs of alcoholic deterioration and dependence. While the articles by Spencer Shaw and Michael Phillips indicate that progress is being made in the detection of biological markers and in the monitoring of alcohol consumption, we are still not even sure how sensitive these markers are to ethanol dosage itself.

A final level of analysis, discussed in section VI, deals with prognosis, natural history, and treatment outcome. These papers attest to the fact that we are moving toward a more coherent approach to treatment efficacy research. In part the impetus has come from a loose coalition of consumers, insurers, politicians, funding agencies, and health care professionals. As alcohol treatment programs proliferate within the health care system, greater accountability is being demanded. The question is straightforward: Should public money be spent on any diagnostic, therapeutic, or rehabilitation procedure for which there is no demonstrable evidence of efficacy? It is therefore not surprising that evaluation research has emerged as one of the most important areas of alcohol studies. For it is here that the methods of evaluation will be tested. It is here that the usefulness of our typologies will be tried. And it is here that the future of alcoholism treatment may well be decided.

It is obvious from this introduction that a hallmark of these papers is their interdisciplinary flavor. Because alcoholism has such a diverse nature it readily invites the application of new disciplines to its study. Nowhere is this more apparent than in the professional affiliations of the present contributors. While medicine still reigns supreme, a host of younger disciplines have become its allies, if not competitors. These include biochemistry, behavioral genetics, pharmacology, neurology, psychology, sociology, and epidemiology. Even more impressive than the methodological contributions these disciplines have brought to the field of alcohol studies is the fact that it is not uncommon now to find their adherents gathered under the same roof in the interest of communication or collaboration. In an era when science and medicine have become increasingly fragmented and overly specialized, alcohol studies seem to offer a common meeting ground for a diversity of professional interests.

This was not always the case. Indeed, at one time the same group of researchers might have been likened to the fabled "Blind men of Hindustan." Chancing upon different parts of the same elephant, each sought to describe the phenomenon from his own limited perspective. The physician "saw" only physical disease, the psychoanalyst only dependency needs; the psychologist reported psychopathology, and the social worker described family conditions. While we are not too far removed from this kind of professional myopia, it is clear that in broadening its intellectual base, alcohol research has also made significant advances in the areas of interdisciplinary collaboration and cross-disciplinary fertilization.

Even a cursory reading of these papers will indicate that the study of alcoholism is in a state of ferment. Whether this process results in wine or vinegar remains to be seen.

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SESSION I: PROBLEMS OF QUANTIFICATION

THE NCA DIAGNOSTIC CRITERIA: 10 YEARS LATER

E. Mansell Pattison

This paper assesses the diagnostic criteria published in 1972 by the National Council on Alcoholism (NCA) as a quasi-official document (NCA 1972). Given the ambitious goal of providing "a set of generally agreed upon criteria for the diagnosis of alcoholism," and widespread publicity and distribution of the document, we might reasonably expect extensive use and evaluation of these criteria. In fact, several unexpected results have occurred: (1) There is almost no documentation of their actual use; (2) there has never been an explicit review of the document itself published, to my knowledge; (3) there have been fewer than a handful of evaluative studies of the criteria; and (4) in contrast, there has been a wealth of sophisticated diagnostic and criterion studies published since 1972—without reference to the NCA document. It appears that the NCA diagnostic criteria have had little impact on the field of alcoholism, and have been generally ignored.

Therefore, it is timely to review these criteria to assess their advantages and disadvantages, to analyze the extant data on the criteria, to evaluate the utility of the criteria from an empirical standpoint, and to assess alternative diagnostic and criteria strategies in comparison with the NCA document.

Description of the NCA Diagnostic Criteria

The first question we may pose is what the criteria are set to determine—to what do they refer? In psychometric terms, this evaluation involves "construct validity." What is the "construct" or definition of alcoholism to which the criteria items refer? Definitions of alcoholism vary widely, so this question is by no means moot. Unfortunately, however, amidst a rambling and prolix discussion in the prolog of the document, no explicit construct appears as referrent for the criteria. This lack immediately poses a scientific problem—how to assess construct validity through appropriate psychometric evaluations when there is no construct.

We can infer a construct from both the discussion in the document and the nature of the criteria items. Or we might infer a construct from the ideological positions of the sponsoring body, the National Council on Alcoholism. However, neither inferential strategy may do justice to the actual intent of the authors and sponsors. The closest approximation to an explicit construct of the official definition of the NCA criteria has been written by Dr. Frank Seixas, chief architect and proponent of the document (Seixas 1975).

> Alcoholism is a chronic, progressive, relapsing disease often ending in death, characterized by tolerance to the effects of alcohol, the presence of a withdrawal syndrome and/or the presence of physical complications of alcohol. (p. 295)

From a technical point of view, we cannot argue with that definition.

One can define a construct and then proceed to devise methods to measure or assess the construct. Thus, we can assess the NCA criteria in terms of this definition, and simply ask whether the criteria can be used as reliable and valid measurements of the construct as stated.

This tactical maneuver is admittedly a narrow view of the diagnosis of alcoholism, but it is legitimate. If the NCA criteria accomplish this task, the document is valuable for that specific purpose.

A quite different question is whether we wish to limit the construct of alcoholism to this narrow definition. Furthermore, if we decide to extend or redefine this construct of alcoholism, we must then determine the construct validity and utility of the NCA criteria items for that construct.

Rationale of the NCA Document

The reasons cited in the prolog for developing the diagnostic criteria are primarily social, political, economic, and legal, rather than scientific or therapeutic. The document implies the need for diagnostic criteria to justify the designation of alcoholism as a disease, and to justify the diagnosis of specific persons as having that disease. The ultimate end of this rationale is humanitarian: To support the development of more humane and effective treatment of alcoholics in our society. However, the implications of the rationale are profound for the actual development of the diagnostic criteria when the intent is first and foremost to buttress social acceptance of alcoholism as a disease. The criteria might well meet that need, yet not meet scientific or therapeutic needs because those are secondary goals for the criteria. I propose that this interpretation is plausible, because, as we shall see, the criteria items are indeed skewed to justify a "medical diagnosis" of a "disease."

This rationale is elaborated in the document, where alcoholism is described and defined as a "disease," and the idiom of "disease" is reflected throughout. Elsewhere, Seixas (Kaim et al. 1977; Seixas et al. 1972) has justified the document as an aid to physicians making medical diagnoses of patients within the medical care system.

At issue here is not whether it is legitimate to label or define alcoholism as a disease. Most of us in the alcoholism field would certainly support such a denotation. Rather, the issue is whether this rationale in the minds of the authors significantly influenced the conceptual framework of the diagnostic criteria, and if so, how?

Purposes of the NCA Document

The prolog of the document sets forth six purposes for which the diagnostic criteria may be used. Not all of the purposes are weighted equally, however.

First, the criteria may be used to extrapolate back from a cluster of symptoms to ascertain the nature of the disease. This definition is not considered a main goal of the criteria.

Second, they may be used to provide a standard nomenclature. This goal is considered major.

Third, they may be used to promote early detection, but no weight is assigned.

Fourth, they may be used to prevent overdiagnosis; this goal is considered very important.

Fifth, they may be used to determine treatment. This goal was considered important, but beyond the scope of implementation.

Sixth, they may be used to determine prognosis. This goal is stated to be obscure.

Despite the wide range of stated purposes, the document does not explain how to use the criteria for those purposes. Seixas and others on the committee (Kaim et al. 1977; Seixas et al. 1972) admitted this omission in discussions, but stated that they had expected investigators in the field to develop these aspects. Since the stated purposes cannot be accomplished by the criteria as published, we may explore some inferential purposes of the document.

The prolog stated that "the main initial use is expected to be for the identification of individuals at multiple levels of dependency," and "to include material which would differentiate degrees of severity, and to allow for progression of the disease, where it exists."

These purposes indicate that the criteria should provide differential assessments of levels of dependency, degrees of severity, and extent of progression. Yet again, no mechanisms in the document specifically accomplish these purposes.

Finally, the prolog concludes unequivocally: "Our intent is rather that the person who is asked to carry definite diagnosis of alcoholism, *surely* fit into that category."

In sum, then, the purpose of the diagnostic criteria is very precise and narrow, designed to produce one explicit result: The person diagnosed is, unequivocally, an alcoholic. That is the sum product of the diagnostic criteria, to serve as a simple binary model of decisionmaking. The answer is either yes or no. It is noteworthy that despite a broad set of stated purposes and resulting differential assessments, the actual diagnostic outcome is quite simple.

Again, from a technical point of view, a simple binary diagnosis of an alcoholic in accord with the stated construct is an acceptable goal of a set of diagnostic criteria. Yet the conceptual issues involved in criteria limitations must be raised.

First, what are the advantages and disadvantages of such a narrow binary decision? Second, how effective are the criteria in reaching this decision? Third, how comparable are the NCA criteria versus other criteria for reaching the same decision? Fourth, if one wishes to use the criteria to achieve the other purposes outlined, what is their utility beyond the binary decision?

Structure of the Diagnostic Criteria

There are 86 descriptive terms, organized into two tracks: Track I contains physical and laboratory items and Track II contains behavioral, psychological, and attitudinal items.

Each item is given a weight of 1, 2, or 3 in terms of diagnostic significance. Group 1 items are classical, definite, or obligatory. A person who meets these criteria must be diagnosed as alcoholic. Group 2 items are probable, frequent, or indicative. A positive item indicates strong suspicion of alcoholism; other corroborative evidence should be obtained. Group 3 items are potential, possible, or incidental. They are common manifestations of alcoholism and should arouse suspicion, but other significant evidence is needed to make a diagnosis.

Items are separated into major and minor criteria, but "major" and "minor" are not defined even though meeting a "major" criterion item justifies a diagnosis of alcoholism. Note, however, that many major criteria items are given a diagnostic weight of 2. This rank seems illogical, in that a major item is, by definition, an "obligatory" diagnostic item; a weight of 2 is only "probable." Finally, minor criteria items are further segregated into early, later, and late stage diagnostic items.

A diagnosis of alcoholism is made if one or more major criteria exist, or if several minor criteria exist in both Tracks I and II. No definitions are given of what *several* means, or *how many* in each track, or what combination or permutation of criteria is sufficient evidence.

It is clear that the diagnostic criteria do not form a psychometric instrument, but are, rather, a collation of data from which the diagnostician must form a decision. Thus, the section on diagnosis states,

> A mechanical selection of items is not enough, and an attempt to fit the history and physical examination and other observations, plus laboratory evidence, into a consistent whole, must be made to ensure a proper diagnosis.

Therefore, the diagnostic criteria are not diagnostic criteria; rather, they are informational items, which can be used in making a diagnosis. In and of themselves, the items do not justify a diagnosis, regardless of whether they are major or minor criteria, and regardless of the diagnostic weighting. Or as Jacobson (1976*a*) states,

> The NCA criteria are viewed as a useful tool for structuring an alcoholism-

> related history and physical—which must be done on an individual basis by a trained physician. (pp. 129-130)

We must conclude that the NCA criteria are useful, in that they list informational items that guide diagnostic and evaluative decisionmaking. In terms of accuracy, however, it is imprecise and inaccurate to call the document diagnostic in the sense of psychometric criteria.

The NCA criteria list signs and symptoms, as elsewhere in medicine are lists of signs and symptoms of other diseases and syndromes. Again as in medicine, however, signs and symptoms are not necessarily the same as definitive and obligatory diagnostic criteria. In medicine, there are signs and symptoms for most diseases. In some instances, the signs and symptoms may be identical for a disease with different etiologies. For example, the signs and symptoms of pneumonia may be identical, even though the etiology may be different, such as for pneumonia due to bacteria, virus, parasite, or congestive heart failure. Generic diagnosis of the condition of pneumonia is satisfactory to determine that a person is sick and in need of treatment. However, the generic diagnosis, based on the signs and symptoms of pneumonia, is inadequate and insufficient to provide necessary and appropriate treatment. Thus, definitive criteria, which establish the etiology of the pneumonia, are required; the same type of criteria are necessary for alcoholism and are not present in the NCA document.

On the other hand, there are many syndromes in medicine in which signs and symptoms are the only available diagnosis because specific etiologies have not been determined, or cannot easily be determined. In some such instances, as with a common cold or influenza, generic treatment methods may suffice, and the search for definitive diagnostic criteria is of no practical import. Or we may have a syndrome such as senile dementia, in which multiple factors interplay to produce a clinical syndrome. Here, specific diagnostic criteria cannot yet be provided. However, treatment of senile dementia can be effectively instituted to rectify known factors, such as nutrition, perceptual deprivation, social deprivation, and remediation of physical complications, that may contribute to the syndrome. Thus, one can use diagnostic criteria to begin treatment.

The NCA diagnostic criteria are presented with conceptual confusions about signs and symptoms versus definitive and obligatory diagnostic criteria, definitive diseases versus syndromes, and the difference between etiological and treatment diagnoses in syndromes.

The document does discuss alcoholism as a syndrome in some places, and elsewhere treats alcoholism as a specific disease with obligatory diagnostic criteria. As a result, the items themselves and the diagnostic instructions are conceptually confused. The actual items are collated signs and symptoms that can appropriately be used to diagnose a syndrome, and the document itself acknowledges that there is no one obligatory set of criteria. Yet the instructions read as if one is indeed using a set of obligatory diagnostic criteria to define a specific entity. In fact, that is not what the items provide, nor is that what the diagnostician using the instrument does.

In sum, just in terms of their own internal logic, the NCA diagnostic criteria can be legitimately used as a laundry list of signs and symptoms, from which the diagnostician can proceed to make the diagnosis of a syndrome of alcoholism. As structured and presented, however, the NCA diagnostic criteria cannot be used either to provide obligatory diagnostic criteria or to diagnose a specific disease entity.

Let us return to the case of pneumonia. The set of signs and symptoms provides justification for the diagnosis of the syndrome of pneumonia, which legitimizes the person as ill with pneumonia, and thus justifies treatment. Here is the binary diagnosis of presence or absence of pneumonia. But the utility of making this diagnosis is neither therapeutic nor scientific. It is social and economic. A more complex and sophisticated process must be constructed to deal with the scientific and therapeutic diagnosis. So it is with the NCA diagnostic criteria. They provide for a binary legitimizing diagnosis of the syndrome of alcoholism.

Critique of the NCA Diagnostic Criteria

Four advantages of the document seem plausible. First, it provides a reference list of signs and symptoms that can be used when making a diagnosis of the syndrome of alcoholism. Second, it can raise the consciousness of physicians and provide a useful guideline for their consideration of alcoholism. Third, it provides a medical legitimizing diagnosis. Finally, it may have provided an impetus to the field of alcoholism to develop diagnostic methodologies to serve the purposes outlined in the document's prolog.

Having listed the above advantages, we must now consider a series of disadvantages, problems, and inadequacies.

The NCS Construct of Alcoholism Versus the Syndrome

The construct of alcoholism used in the NCA document is *one* pattern of alcoholism and is a legitimate construct. The problem, however, is that it is not the only pattern of alcoholism in terms of development, chronicity, recurrence, or prognosis. Further, the construct includes the presence of tolerance, withdrawal symptoms, and physical complications. In many cases, none of these three needs to be present to make a clinical diagnosis of alcoholism. Thus, the NCA criteria establish only one specific type of alcoholism pattern to be diagnosed.

Second, there is an implicit assumption in the NCA construct that a specific entity—alcoholism—exists. As Pattison, Sobell, and Sobell (1977) outlined in detail, this "entity" concept assumes that there is a definitive distinction between a class of persons who "have" a specific disease, alcoholism, and who are substantially different from problem drinkers, heavy drinkers, prodromal alcoholics, and so on. That concept has been generally discarded by much of the scientific community in the light of research data, which fail to demonstrate a unique entity of "alcoholism," while indicating a continuum of dysfunctional alcoholism patterns. As Rohan (1976) commented,

> The results show that the label alcoholic subsumes great quantitative diversity and that the present dichotomy of normal vs. abnormal drinker, or social drinker vs. alcoholic should be replaced with a concept of a continuum. The adverse effects of drinking are not linearly dependent on the quantity of drinking but depend on many other factors as well.

The criteria are misleading in setting forth *one* diagnostic task, namely the diagnosis of *one* specific condition. In fact, the diagnosis of alcoholism is the task of discriminating where a person is on a continuum.

Third, the NCA criteria conceptually misuse and confuse the concept of a syndrome. Although the NCA document refers to alcoholism as a syndrome, and even presents the diagnostic task as a collation of signs and symptoms (which taken together may lead to a diagnosis of alcoholism), it ends up abandoning the syndrome concept by providing only one diagnostic conclusion: The person does or does not fit the NCA construct of alcoholism.

Most scientific authorities in the field of alcoholism now concur that alcoholism is a *multivariate syndrome*. That is, there are multiple patterns of dysfunctional alcohol use that occur in multiple types of personalities, with multiple combinations of adverse consequences, with multiple prognoses (Edwards 1977; Edwards and Gross 1976; Horn 1978; Caddy 1978; Davies 1979; Mendelson and Mello 1979; Belasco 1971; Davis and Schmidt 1977; Larkin 1974; Pomerleau et al. 1976; Robinson 1972; Willems et al. 1973; Kissin 1977; Pattison 1974; and Pattison 1979).

Stedman's medical dictionary defined "syndrome" as "a group or set of concurrent symptoms which together can be considered a disease." So the designation of alcoholism as a syndrome in no way affects the legitimate concerns of many professionals who label alcoholism as a disease (Gove 1975).

The importance of the concept of alcoholism as a syndrome is that we then eradicate our search for a nonexistent entity—alcoholism. There is no question that there are "alcoholics," for the label is applied widely to a certain social reality. But the fact that we can describe and diagnose a person as "alcoholic" does not logically imply that there is a specific entity "alcoholism." There is a syndrome of alcoholism, but we may not reify the concept of syndrome into a concrete entity.

Miller (1976) has pointed out that for a diagnosis of alcoholism, the utility of the diagnosis lies in the description of a consistently intercorrelated set of symptoms (i.e., a syndrome) with implications for etiology, prognosis, treatment, and prevention. At issue, then, is the fact that although the NCA criteria move toward a set of criteria for diagnosis of a syndrome, the document fails to treat the criteria items as a collation for a syndrome, and fails to provide for specific implementation of the criteria for the purposes of etiology, prognosis, treatment, and prevention.

The NCA Binary Decision Method

In accord with the above discussion, the next conceptual problem is the binary decision mechanism provided by the document. This binary decision is legitimate, but it poses two major problems.

First, the document asserts the intent to diagnose only those persons who "surely" fit the diagnosis. This maneuver thus excludes many alcoholics on the continuum of the syndrome of alcoholism. So, although the document wants to avoid overdiagnosis, at that same time, it achieves underdiagnosis.

Second, the binary diagnosis is inadequate to provide meaningful data for the many purposes outlined previously. Again, Miller (1976) comments,

> A large amount of information is lost when the data regarding various aspects of the problem are reduced to a binary nomenclature. Certainly this reduction cannot improve our prediction of such complex events as treatment outcome.

The NCA Inferences of Stages of Alcoholism

The document sets forth early, later, and late stage criteria. The implicit assumption is that there are reliable and valid sequences of diagnostic signs and symptoms in the development of alcoholism. Again, this is part of the folk-science model of alcoholism, which Pattison, Sobell, and Sobell (1977) have demonstrated to be unsupported by the extant research. Three significant problems with this stage assumption are presented in the NCA criteria.

First, stage criteria items are listed for minor criteria only, and omitted from the major criteria. In terms of psychometric methods, the omission seems illogical, because it weakens the potential discriminatory power of the major criteria in the evaluation of potential stages.

Second, the NCA document provides no empirical base to support the denotation of specific items as early, later, or late stage signs and symptoms. Without empirical support, we must therefore question the "face validity" of assigning the items to particular stages.

Third, there is substantial empirical evidence to indicate that the discrete sequential ordering of signs and symptoms does *not* occur. For example, Park (1973) reports,

> If there be three phases in the development of alcohol addiction . . . a sizeable proportion of experiences do not occur in the phases to which they are assigned . . . The presumed manifestations of alcoholism do not necessarily develop in the order given by Jellinek.

Similarly, Orford and Hawker (1974) conclude,

> There is a characteristic ordering of new events or symptoms in the development of alcoholism, but we would argue strongly that the extensions of this notion to include a wide range of events encompassing psychophysiological, social, and treatment events is not feasible and has served only to obscure a number of more basic and relatively circumscribed processes.

Thus, the validity of segregation of NCA criteria items into stages is seriously questioned.

The Emphasis on Late Adverse Consequences in the NCA Criteria

It has been noted in published critiques that most NCA criteria items refer to severe consequences of drinking, usually manifested after many years of heavy, prolonged, and deleterious drinking (Kaim et al. 1977). Although this strategy increases the "surety" of diagnosis, and conforms most closely to the NCA construct of alcoholism, it also serves to exclude and minimize the utility of the criteria both to diagnose less severe and prodromal syndromes and to detect alcoholism in earlier phases of development.

Proportionate Emphases in Track I and Track II

The prolog of the document notes that the behavioral manifestations of alcoholism "may be the easiest to determine and most objective to recognize." So we might anticipate psychological and behavioral items to be stressed as major criteria.

In fact, in terms of major criteria, just the reverse occurs. In Track I are 23 major criteria, all of which are physiological and physical, and all are indirect consequences of drinking. The Track II major criteria are only labeled psychological dependence; there are only three, and none pertains directly to psychological dependence.

Thus, the major criteria overwhelmingly emphasize the indirect physical consequences of drinking, even though the document itself states that the psychological and behavioral components of alcoholism are the easiest to determine and objectively recognize. And these are almost totally excluded from the major criteria. The omission seems internally inconsistent in the document, illogical, and symptomatic of a weak psychometric methodology.

The Logic of Allocation and Weighting of NCA Criteria Items

The document provides no clinical or empirical justification for either the allocation of items into major or minor criteria, or the diagnostic weighting of each item. Thus, there is questionable "face validity" to the assignment and weighting of items.

Further, there are many logical inconsistencies in the assignments. For example, Kal (1973) observed,

> It would seem to follow that all "major" criteria are those of level 1 (and vice versa). Yet in examining the tables one finds that several major criteria are weighted as 2 or 3, and some minor ones as 1. This leads to the paradox that a person with beriberi "who drinks regularly" . . . should be considered as *possibly* alcoholic, both by virtue of the indicated level 3 weighting and, in my opinion, by the very nature of the case. Yet at the same time, this criterion alone suffices for the *definitive* diagnosis of alcoholism because it is a major one! Several other examples can be found by examining both tables.

The Specificity of NCA Criteria Items

From a psychometric point of view, it is desirable that items be selected that are specific to alcoholism, and not signs and symptoms found in other states. However, 14 of 25 major criteria in Track I are nonspecific. And for the minor criteria, 32 of 35 Track I criteria are nonspecific as are 24 of 27 behavioral items in Track II. Furthermore, most of the *specific* alcoholism items that have been elucidated elsewhere are omitted from the document.

Another issue of item specificity is the differentiation between signs and symptoms of acute alcohol ingestion, the direct effects of prolonged alcohol ingestion (both physical and psychological), the consequential effects of drinking behavior, and nature of the drinking behavior itself. Although items in the NCA document refer to each of these different categories, they are not logically organized for either clinical or psychometric evaluation.

The Preciseness of NCA Criteria Items

Most of the criteria items are general descriptive statements; few, if any, have a *quantitative* dimension. Thus, there is a high degree of imprecision in item construction, which can produce ambiguity, difference in interpretation or valuation, and, most important, an inability to rank or quantify the items. Thus, the items are psychometrically unsuitable in their present form. However, the present state does not mean that the items cannot be framed in scaleable and quantifiable form; indeed some investigators have done so.

The Diagnostic Suitability of NCA Criteria Items

Several of the major criteria items, such as alcoholic cerebellar degeneration, central pontine myelinolysis, and Marchiafava-Bignami's Disease, can be ascertained only in postmortem examinations. Such items, of course, are not useful in a clinical diagnosis.

The Reliability of NCA Criteria Items

Although an item may be valid, it may not be reliably replicable either because of the variability of the observer or of the informant or because the content of the item itself is so highly variable. No data are given in the NCA document on item reliability, even though many items have been shown to be highly unreliable in other studies.

The Covariance of NCA Criteria Items

In the alcoholism syndrome, it is important to determine the permutations that have different predictive values. To do so requires a diagnostic instrument from which we can derive psychometric intercorrelated clusters of signs and symptoms, each of which becomes a subtype of the syndrome. However, we have already noted that the NCA diagnostic criteria were not intended to serve this goal. Furthermore, the instrument is not constructed to facilitate psychometric analysis of item sets. Finally, the NCA document provides neither mechanisms nor data referrents to cluster analysis of the items.

The Discriminant Validity of NCA Criteria Items

One of the important values of any diagnostic test is its discriminant validity—that is, its ability to discriminate between the target construct and other constructs or states. Construct validity is related to the specificity and precision of items, as well as to the validity of the items as construct referrents. The discriminant validity is reflected not only in the capacity of the instrument to correctly identify the construct, i.e., alcoholism, but also the proportion of false negative and false positive results. The NCA document provides no data as to discriminant validity, although we might surmise the validity to be low, based on the prior problems of psychometric methodology identified.

From a psychometric view, it is methodologically desirable to determine the discriminant validity of individual test items; low validity items will lower the overall validity of the instrument. An effective psychometric instrument requires appropriate statistical evaluation of preliminary item sets to eliminate spurious items. This evaluation has not been performed on the NCA criteria. Thus, we do not know the degree of redundancy, nor the saliency, of items.

The Content Construction of NCA Criteria Items

From a methodological standpoint, criteria items should be constructed on the same conceptual scheme. But the NCA document indiscriminately mixes different conceptualized items. Jacobson (1976) notes that the items include

> Physiological and clinical signs and symptoms, physical disorders, laboratory tests of blood and urine, observable behaviors, and those reported by the proband or the family, and inferential material.

Thus, the items are not comparable in either qualitative or quantitative terms.

The Comparative Effectiveness of NCA Criteria Items

Although the document may provide an accurate diagnosis, we need also to determine its comparative effectiveness. I refer to its accuracy, compared with other diagnostic instruments; its bias toward administrator or client, compared with other instruments; and its utility of administration in terms of cost in administrator and client time, adjunct test costs, and types of personnel required to administer the instrument in what settings.

The NCA document does not provide any data on its psychometric qualities of comparative effectiveness. In terms of the more general attributes of comparability, the NCA document is relatively costly and cumbersome. Jacobson (1976) observes:

> Since most of the criteria necessitate a physical examination, or laboratory tests, or medical anamnesis, it is unlikely that persons not trained in medicine would be able to appropriately utilize the major portions of the criteria . . . . Both the major and minor criteria of Track II require a skill in anamnestic

> methods that exceeds that possessed by many alcoholism workers . . . . The criteria could involve a half-hour to forty-five minutes of the user's time at a cost . . . excluding all but the most common and rudimentary laboratory work.

Finally, Jacobson (1976) sums up his estimate of its comparable effectiveness: "Attempts to apply the entire criteria would be so expensive and time-consuming as to be totally impracticable."

Summary of Critique

Although the document presents a legitimate and useful diagnostic schemata, the diagnostic intent is narrow in scope and low in utility. The document has major conceptual limitations; major psychometric deficiencies in logic, concept, and construction; and undefined reliability, validity, and comparative effectiveness. Its general utility appears severely limited on numerous counts.

Assessment of the NCA Diagnostic Criteria

Few direct or even indirect studies have been published in relation to the document. The few studies available illustrate and document some of the problems and issues raised in the critique.

The issues of item reliability were tested by Holland et al. (1979), who found that items such as causes of drinking, psychological reasons for drinking, decreased tolerance reports, welfare or disability status, and usual times for drinking are all quite unreliable. All of these items appear as NCA criteria. Similarly, Stein and Bowman (1977) found that measures of escape or symptomatic drinking were insignificantly related to drinking patterns or consequent behavior.

The issue of item validity is raised in a study by Justin (1979) on routine breath analysis for alcohol, which is weighted as 2 (probable alcoholic) in the NCA criteria. In 535 consecutive outpatients, Justin found six positives: one due to mouthwash, four nonalcoholics, and one alcoholic. Meanwhile, he clinically diagnosed 22 alcoholics in the series, none with positive breath analysis. This study illustrates many of the problems of reliability, validity, and discriminant analysis of the NCA items.

The problem of the heavy emphasis given to physical criteria in the NCA schemata is illustrated by two different types of investigations. First, Breitenbucher (1976) examined 70 identified alcoholics. Only 27 were identified by clinical medical examination, 43 were identified by the MAST self-report, and only 5 of 70 had physical criteria matching the NCA diagnostic criteria. Second, a series of papers by Drum and Jankowski (1977, 1978; Jankowski and Drum 1977, 1978) explicitly used the NCA criteria. The only consistent physical and laboratory NCA items present in the majority of alcoholics were two laboratory findings: liver histopathology and erythrocyte macrocytosis, and these were found only in severe chronic alcoholics. Although the authors could increase their positive identification of alcoholics to 99 percent through an extensive battery of tests, such cases were hospitalized only for severe cases of alcoholism. More important, this battery also produced up to 40 percent false positives! Their study illustrates the limitations of the undue dependence of the NCA criteria on physical criteria items.

The problem of lack of item precision is illustrated in a study of eight different measures of alcohol consumption by Streissguth et al. (1977). They report low intercorrelations between the eight scales, and each scale tended to detect different types of alcohol consumption. Thus, even with sophisticated scaling methods, we still do not have an acceptable diagnostic measure based on alcohol consumption, and the NCA criteria provide no quantitative scaling. This factor points up the inadequacy of the NCA criteria for precise diagnostic assessment.

The problems of item reliability and discriminant validity were specifically assessed on the NCA criteria by Ringer et al. (1977). They found that 38 of the 86 items were not discriminatory. They did identify their alcoholic sample at 99 percent accuracy, but they also had a 47.5 percent false positive identification of controls!

Although a physician sample has provided face validity concurrence with the NCA criteria items (Filstead et al. 1976), their findings do not meet more precise psychometric requirements.

An attempt to use and quantify the NCA criteria items is reported by Landeen et al. (1977). They clustered 9 major and 27 minor criteria. Their experimental sample consisted of severe chronic alcoholics. Given this population, they were able to use either the major or minor criteria to discriminate alcoholics at a high level of statistical significance. However, in comparison, the simple self-report brief BMAST test was just as effective as a diagnostic instrument. Furthermore, in a sample of 60 alcoholic patients, the BMAST produced only four diagnostic errors (6 percent), all false negatives. Using the major criteria resulted in 11 diagnostic errors (18 percent)—10 false negatives and 1 false positive. Using the minor criteria produced 20 diagnostic errors (33 percent), 15 false negatives, and 5 false positives. This study is particularly instructive, for it demonstrates that the NCA criteria can be quantified. However, even with a very select population of alcoholics matching the NCA construct of alcoholism, the NCA criteria have high rates of false negative and false positive diagnoses. More important, a simple quick test such as the BMAST is much more accurate.

In sum, available studies do not support the utility of the NCA diagnostic criteria. These studies demonstrate the problems with validity, reliability, and discriminant power of the criteria items; illustrate the skewed bias toward physical consequences (which do not have high diagnostic utility); and reveal that the NCA diagnostic criteria are neither intrinsically accurate nor even as accurate as simpler instruments.

Alternatives to the NCA Diagnostic Criteria

The above critique and assessment leads to the conclusion that the NCA diagnostic criteria are on the one hand useful, and on the other hand, limited, so we must consider alternatives. If nothing better is at hand, then it is appropriate to recommend the use and extension of the NCA document. However, if other methodologies and instruments that retain the advantages and avoid the disadvantages of the NCA diagnostic criteria are available, there seems little justification to perpetuate the NCA criteria.

First, there are several major reviews of diagnostic instruments that provide a binary diagnosis—the NCA diagnostic criteria. Without detailing the myriad tests, it suffices to conclude that brief paper-and-pencil self-report or brief interview instruments are available. They have acceptable reliability and validity, and equally acceptable or better discriminatory power than the NCA diagnostic criteria (Knox 1976; Neuringer and Clopton 1976; Jacobson 1976; Kaplan et al. 1974).

Second, significant research has been attempted to develop precise measures of different cluster components of the alcoholism syndrome. These include neuropsychological discrimination (Tarter 1976); quantifiable measures of alcohol consumption related to clinical patterns (Little et al. 1977; Khavari and Farber 1978); measures of involvement with drinking behaviors (Gillies et al. 1975; Hilton and Lokare 1978; Shelton et al. 1969; Bowman et al. 1975); measures of patient characteristics as diagnostic indicators (Ogborne 1978); measures of sociodemographic diagnostic predictors (Hart and Stueland 1979*a*, *b*); differential assessment of indexes of stages (Mayer and Filstead 1979; Mulford 1977); and measures of change (Stallings and Oncken 1977).

The most important advance, however, is the development of psychometric methods for clustering the signs and symptoms of the alcoholism syndrome into useful predictive subtype clusters. These groups, then, can be used for epidemiological research, treatment prescription, and prevention. Major significant methods and instruments of this type have been separately developed by Marlatt (1975), Wanberg et al. (1977), Horn (1978), Cronkite and Moos (1978), and O'Leary et al. (1979). Their sophisticated methods are not easily applied to the clinical situation and that remains to be done. Pattison (1980) and Bhatia (1979) have made some initial attempts, but they should be considered as first clinical steps toward a more sophisticated clinical methodology.

Conclusions

This analysis of the NCA diagnostic criteria has noted the relative lack of use of the document and the lack of research pertinent to the instrument. A critique and assessment of the document reveals major conceptual, methodological, psychometric, and utilitarian problems, which may explain why the document has received relatively little attention.

Although the document presents a legitimate diagnostic approach, it is narrow in scope and severely limited in applicability. Other diagnostic instruments accomplish the same diagnostic task as the NCA diagnostic criteria, but have more desirable psychometric qualities and are more utilitarian. Finally, more sophisticated methodologies, with the requisite psychometric and conceptual flexibility to deal with the data, have been developed, rendering the NCA diagnostic criteria document obsolete.

In conclusion, we might appropriately regard the NCA diagnostic criteria as somewhat like a Model T Ford—still around, still usable, but of limited range; appreciated as one of the first useful models, but superseded by better models and better technology.

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THE DRINKING HISTORY: PROBLEMS OF VALIDITY AND RELIABILITY

G. Alan Marlatt

This paper discusses some of the issues related to the assessment of drinking behavior (and the diagnosis of alcoholism) based on self-report data. Self-report data are often obtained during the taking of a drinking history, in which individuals are asked to describe or indicate (using checklists of symptoms, for instance) their drinking patterns and the effects of their drinking on a range of personal and social variables. Of central concern to this topic are the twin issues of validity and reliability: How accurate is the information obtained in the drinking history, and how stable or reliable is this information over various time periods?

The answers to the questions of validity and reliability are significantly influenced by the underlying theoretical orientation of the diagnostician. Currently there are two major conflicting theoretical models of alcoholism. Some professionals perceive alcoholism as a disease, and seek information designed to arrive at a diagnosis of the patient's disorder. Other investigators (including this author) are concerned with providing descriptive information about an individual's drinking behavior and any associated problems the drinker experiences. From this latter perspective, problem drinking is viewed as a learned disorder rather than as a disease state.

These two positions lead to quite different assessment strategies, so it seems worthwhile to examine and compare each approach in some detail. This paper, therefore, describes each model in turn, and discusses how both orientations might differentially affect the validity and reliability of the drinking history. The paper concludes with a brief review of research and related issues in the recent literature on self-reports of drinking behavior.

The Traditional Disease Model and the Diagnosis of Alcoholism

The traditional disease model assumes a dichotomous distribution of alcohol-related problems. The overall goal of the diagnostic process is to assign the individual to one of two discrete categories: Alcoholic or nonalcoholic (the latter category is often subdivided into social drinker and abstinent groups). A similar dichotomy emerges in the assessment of treatment outcome, in which the alcoholic patient is judged to be either abstinent or relapsed.

The basic theoretical assumptions underlying the traditional diagnosis model stem from the notion of alcoholism as a unitary disease entity: The patient either has the disease (or is in some prodromal phase of its development) or does not have it. There have been a number of detailed commentaries on this issue (Jellinek 1960; Pattison et al. 1977). In terms of self-report measures, the diagnosis of alcoholism within this context is usually made on the basis of a *threshold* series of criteria: Once the patient has been found to have a sufficient number of signs or symptoms, that individual is thereby "over the threshold" and can be classified as alcoholic.

From this perspective, the underlying questions to be answered take the following form: How do we know when individuals are "alcoholics"? Are they or are they not? This approach often leads to the development of the checklists or questionnaires frequently seen in publications such as *Reader's Digest* under the title, "Are You an Alcoholic?" ("If you answered yes to eight or more of the above items, you should seek professional help for your alcoholism problem.") Here, the emphasis is on the *diagnosis* of alcoholism; as with most diseases, the person either "has it" or doesn't, although an attempt is occasionally made to further define the particular "stage" of alcoholism the individual is in.

The Michigan Alcoholism Screening Test, MAST (Selzer 1971), is currently the most widely used diagnostic screening instrument of this type. The MAST consists of a series of 25 questions to be answered either yes or no by the respondent. Sample questions include "Do you drink before noon fairly often?" and "Do you ever feel guilty about your drinking?" Each item is assigned a weight between 0 and 5; responses are totaled, and a score of 5 or higher is considered evidence of alcoholism (threshold cutoff score). In addition, certain items are considered directly diagnostic of alcoholism; for example, a positive response to the item, "Have you ever attended a meeting of Alcoholics Anonymous?" is assigned a score of 5, sufficient to put the respondent over the threshold. (It is curious to note that an affirmative response to the item, "After heavy drinking have you ever had delirium tremens or severe shaking, or heard voices or seen things that weren't really there?" receives only a score of 2 in this scoring system.) The MAST has been widely used as a screening device in a variety of applied settings, either in the full 25-item version, or in one of two recently developed shorter versions that contain fewer than 15 items (Pokorny et al. 1972; Selzer et al. 1975).

MAST and similar screening instruments have a number of obvious shortcomings. Because of the high face validity of the items, it is easy for a respondent to falsify responses if so desired, thus weakening the validity by scoring a high rate of false negatives. Research concerning the reliability and validity of the test has been minimal to date, and the overall results so far have been mixed (Jacobson 1976). Most of the studies have examined the internal consistency of the test (e.g., Zung 1979) and have not directly addressed the issues of validity or reliability. The biggest problem to overcome in validity studies, of course, is to establish firm criteria for the independent diagnosis of alcoholism, in order to provide a standard comparison with the MAST predictions. So far, no such generally accepted set of diagnostic criteria exists: In a review of traditional diagnostic procedures, W.R. Miller (1976) concluded that there is little consensus as to the definitive criteria for the diagnosis of alcoholism. The search for criteria associated with a unidimensional definition of alcoholism is probably doomed to ultimate failure, given recent evidence strongly suggestive of the *multidimensional* nature of alcohol problems (e.g., Pattison et al. 1977). Recent factor analytic studies of the MAST itself support this view; the results show the test to have a multifactorial structure rather than the single "alcoholism" factor predicted by the unidimensional model (Friedrich et al. 1978; Zung 1978).

Threshold diagnostic instruments such as the MAST are limited primarily by the fact that they yield on a binary yes or no outcome, and tell us virtually nothing about the frequency, variability, or pattern of the respondent's drinking behavior (see Kaplan et al.

1974). A careful reading of the MAST items suggests that the test may be tapping into a global index of perceived *control* or personal concern over drinking as expressed either by the respondent or by others in the immediate environment ("Do you feel you are a normal drinker?" "Can you stop drinking without a struggle after one or two drinks?"). Many of the items call for the respondent to make some kind of subjective judgment or evaluation of drinking, rather than to provide an objective or value-free description of the behavior. By asking respondents to evaluate or judge the "normality" of their behavior, or to query them about the extent to which they feel they can exercise control over their drinking, is to invite a defensive reaction such as denial, rationalization, or other distortion strategy. This point becomes even clearer if we substitute the term "drinking," with its inherent negative value associations, for another more positively associated behavior such as skiing. Skiing is a good example to use in this respect, in that it has sometimes been defined as a "positive" addiction (for instance, Glasser 1976). We recently constructed an instrument called the "Banff Skiism Screening Test" to further illustrate this point (Miller and Marlatt 1977). Here are a few sample items: "Do you ever ski in the early morning?" "Do you ever find that once you start skiing you are unable to stop?" "Do you find that it takes progressively stiffer slopes to satisfy you?" There are 18 items in all, along with a handy diagnostic interpretation guide. (Scores of 10 to 12 indicate a "skizoid" condition.)

The Social Learning Model and the Assessment of Drinking Problems

The social learning model (Bandura 1969, 1977) and its applications to the alcoholism field (for instance, Marlatt and Nathan 1978; P.M. Miller 1976; Miller and Mastria 1977; Nathan et al. 1978) basically assume that drinking is a learned behavior, one that ranges along a *continuous dimension* of alcohol consumption. From this perspective, there is no clear line of demarcation between the social drinker and the "alcoholic"—instead, there are various degrees of drinking-related problems that people may or may not experience. Instead of a dichotomy between those who have the disease "ism" and those who do not, there is the assumption that there are many types of social drinkers (light, moderate, heavy, and so on; see Cahalan et al. 1969), and many potential problems that may befall the drinker (health, family, economic, moral).

Social learning theorists, rather than asking "What is alcoholism?" or "Is this person an alcoholic?", prefer to ask the following types of questions: "How can we describe the pattern of this person's drinking behavior?" "What are the antecedents and consequences of this person's drinking?" "Under what conditions was this drinking problem acquired, and how is it maintained?" "What factors can be manipulated to change this person's drinking habits?" Treatment outcome is assessed along a similar dimension, ranging from total abstinence through various degrees of resumed drinking. Someone who shows a significant reduction in drinking following treatment would not be equated with someone else who shows no improvement; they are not in the same "relapsed" category.

The overall approach to assessment is quite different from the social learning perspective because of the emphasis on the person's behavior, or on an assessment of what the person is *doing* (with regard to both drinking and its consequences), rather than on some underlying state that serves as an index of what the person *is* (that is, alcoholic or not). In the traditional disease model, the person is equated with the disorder (you *are* an alcoholic); the social learning approach attempts to objectively describe the person's behavior, separate or detached from the basic self-image. We don't label someone who has cancer as a "canceric"; why should we then label someone who drinks to excess as an alcoholic? By working with clients as "cotherapists" or "colleagues," supporters of the social learning approach hope to encourage a sense of cooperation or openness in which clients are free to discuss their drinking behavior (as opposed to viewing their behavior as a symptom of their status as an alcoholic). By making this distinction between the behavior and the self clear ("Let's you and I look carefully at what you are *doing* and how it's affecting your life"), it is possible to reduce considerably the personal guilt and associated denial of responsibility that many problem drinkers feel. The main point I want to suggest, therefore, is that problems of distortion or inaccurate self-reporting and their subsequent impact on the reliability and validity of the information obtained are mediated primarily by the defensive reactions (guilt and denial) provoked in respondents who are asked to draw an evaluative inference about their drinking behavior, and whether or not the behavior is indicative of the diagnostic label of alcoholism. From the social learning perspective, it is not necessary to spend time trying to "break through the patient's denial system" and convince people that they are alcoholic before making an assessment and beginning treatment. Instead, work can begin immediately on identifying a client's pattern of behavior and associated lifestyle as the first step in treatment planning.

Because of dissatisfaction with the traditional diagnostic questionnaires, we developed an instrument for the behavioral assessment of problem drinking. The Drinking Profile (Marlatt 1976) is a detailed, structured questionnaire designed to be administered on an individual basis by a trained interviewer. In addition to a number of detailed demographic items, the instrument contains a variety of questions pertaining to drinking rates and patterns, problems associated with drinking, periods of abstinence, and typical drinking settings. Other items are designed to provide information about alcoholic beverage preferences and estimates of pretreatment drinking levels. A final section contains items in which clients are asked to specify their personal reasons for drinking (both antecedents and consequences) and to respond to questions relating to motivations for past and present treatment and expectations of treatment outcome. Many of the items are qualifiable and can easily be coded for computer analysis. A scoring manual has also been developed for coding and categorizing responses to the open-ended questions. The Drinking Profile has served as a useful guide for treatment planning, in both outpatient and inpatient treatment settings.

In addition to the Drinking Profile, we use a number of additional assessment procedures, including a personal biography (describing the history and development of the drinking problem); ongoing written accounts of the person's current drinking behavior and associated urges to drink in a daily diary format (self-monitoring); a detailed analysis of the client's ability to cope with a number of "high-risk situations" associated with potential relapse (for instance, coping with feelings of anger, social pressures to resume drinking); direct observation of the client's drinking behavior in either analog drinking tasks (the taste-rating task) or in seminaturalistic environments (the simulated bar setting); and an indepth description of the person's general lifestyle (other persistent habits, exercise patterns, social support systems, work patterns, stress-management activities). Details describing these additional assessment procedures are described in a number of recent publications (Marlatt 1978, 1979; Marlatt and Gordon 1979).

Research and Issues Related to the Reliability and Validity of Self-Report Data

It has become obligatory in recent years to state that self-reports of drinking behavior are "notoriously unreliable" and of questionable validity. However, published research, some of which is reviewed in this section, takes issue with this general conclusion. Until recently, the available data suggested only that restrospective accounts of pretreatment drinking histories given by alcoholics are *often* unreliable. One frequently cited experiment (Summers 1970) reported that alcoholics tended to give varying accounts of their pretreatment drinking histories in the course of two interviews given over a 2-week interval. Despite the fact that this study concerned only the reliability between interviews, the study carried the title, "Validity of alcoholics' self-reported drinking history."

Many argue that there are sufficient reasons to doubt both the reliability and the validity of retrospective self-reports given by alcoholics, because of the combined influence of such factors as memory distortions (especially blackouts), bias, and other defensive reactions to the type of information being sought, and response to the demand characteristics of the interviewer and the setting. Because of these limitations, it is frequently recommended that collateral sources of information, including the reports of "significant others" and access to public records, be consulted to substantiate information obtained from an alcoholic individual. Recent research on the reliability of agreements between the alcoholic individual and the collateral informant is reviewed later in this paper.

Should it be concluded that self-report information has no place in the objective assessment of drinking behavior? Neglecting this source of information can cost us our only access to reports of drinking in the absence of other observers. In addition, reports of private, subjective states related to drinking (such as urges or craving states) can be obtained only from self-reports. A more helpful strategy is to perceive self-reports as one of several response measures open to investigators. A comprehensive assessment package thus includes multiple measures of drinking behavior: behavioral observation of alcohol consumption, physiological effects of drinking, measures of cognitive attitudes and beliefs, as well as other self-report data (Donovan and Marlatt in press). Only by adopting a multifaceted approach can we begin to appreciate how these various measures interrelate with each other and whether the various indexes are independent or interdependent.

Information also should be gathered concerning the determinants of reliability and validity of self-report data. In this regard, factors such as the client's motivational state (desire to please the therapist or interviewer, attitude toward abstinence), the influence of experimenter bias or outcome expectancies, and the social desirability of the behavior under study should all be systematically manipulated to determine their individual impact on the accuracy of self-report data.

One study provides a good example of this experimental approach to self-report data. Sobell and Sobell (1975) interviewed a group of outpatient alcoholics about their social and drinking histories. All subjects were interviewed on two separate occasions, 3 weeks apart, with identical critical items imbedded among filler items in both sessions. At the end of the second interview, subjects were provided the opportunity to go back and change any of their responses. To investigate the influence of motivational factors, the subjects were given one of three instructional sets prior to changing their responses to the critical test items. Subjects in one group were told, "I have actually obtained copies of your hospital and arrest records to check the accuracy of the answers you have given in the interviews, so before we end this interview, I'll give you an opportunity to change your answers to certain questions if you want." In this particular study, few subjects chose to change their answers, but the design illustrates one way to investigate potential determinants of self-report data. The authors checked the validity of the reports given by the subjects by comparing the information with official records and documents. Reliability was assessed by comparing the subjects' responses to the same items in each of the two interviews. On this basis, it was found that 92 percent of the responses were reliable, and 86 percent were valid. Only 5 percent of the responses were underestimates; 9 percent were overestimated when compared with objective criteria. The authors conclude that the self-report data obtained in this study "were found to be sufficiently valid to support their use as a primary source of life history data when compared with official records."

Other data show that the reliability and validity of self-report accounts of drinking behavior are generally adequate for both alcoholics and social drinkers. In a general review of the literature on the reliability and validity of self-reports, Armor, Polich, and

Stambul (1978) concluded that measures of drinking frequency are generally accurate for both alcoholic and nonalcoholic populations, although some drinkers in both groups tend to under-report consumption. The study reported that the internal reliability of such self-reports ranged from +0.57 to +0.71. As would be expected, global categories of self-report were found to yield more reliable information than finer, more discrete categories.

The Sobells and their colleagues recently published a series of studies on the reliability and validity of self-report data. In one study (Sobell et al. 1979), male outpatient alcoholics were asked for information about their drinking behavior for the year preceding the contact. Questions concerned daily drinking patterns, alcohol-related incarcerations, and drinking problem history, using a unique time-line follow-back interviewing technique developed by the authors. Without being warned, subjects were reinterviewed 6 weeks later for the same information. The test-retest reliability coefficients were high, ranging from +0.79 (for number of days abstinent, 30 days pretreatment) to +0.98 (for number of days incarcerated 30, 180, and 360 days prior to treatment, and for total life hospitalizations). No attempt was made to determine the accuracy of these reports, however.

In a related study, Sobell and Sobell (1978) investigated the extent to which the population type of alcoholics (voluntary outpatient, voluntary inpatient, coerced outpatient) and the type of information sought (alcohol-related behaviors, behaviors not directly related to drinking, demographic items) affected the validity of the self-reported information. The veracity of answers was evaluated using official records and documents. The results showed that although population type did not significantly affect validity, the type of question did: Significantly fewer invalid answers were given to demographic questions than to alcohol-related or nonalcohol questions (although the overall error rate was less than 10 percent in the latter two categories). The overall pattern of results in this study shows that the information obtained from self-reports was generally accurate.

Many treatment outcome studies use information from significant others or collateral informants as a validity check for self-reports. Two recent experiments have investigated the accuracy of this procedure. In the first study (Maisto et al. 1979), 6-month posthospitalization followup data were obtained from 52 alcoholic subjects and their collateral informants (relatives and friends). Self-reports concerning alcohol consumption and related information were highly correlated when subjects had been either mostly abstinent or mostly intoxicated throughout the followup period. Less agreement was obtained when the subjects' drinking was neither consistently controlled nor uncontrolled, a finding that probably reflects the fact that alternating periods of drinking and abstinence are more difficult to discriminate than prolonged periods of abstinence or uncontrolled drinking. A similar finding was reported earlier by Orford (1973).

In the second study (McCrady et al. 1978), 44 couples in which one partner was diagnosed as either an alcoholic or a problem drinker were interviewed independently (separate interviews for each spouse), and asked to report on the patient's drinking behavior and impairment due to drinking. Initial interviews covered the 30-day period prior to hospitalization, and later interviews covered the 30-day period prior to the followup (at 6 to 8 weeks and again at 5 to 7 months after discharge). The results showed moderately positive correlations between patient and spouse perceptions of drinking behavior, with correlations varying from +0.52 for a specific quantity-frequency index of consumption to higher coefficients (+0.56 to +0.96) for more global consumption indexes. Similar positive correlations were obtained for the impairment index. The authors conclude, "When more global, molar ratings of drinking are derived, agreement improves accordingly."

The most stringent test of the validity of self-report data is to directly compare the subject's own description or rating of drinking patterns and rates with independently derived objective measures of actual drinking behavior (concurrent validity). Several studies have addressed this question. Fine, Steer, and Scoles (1978) obtained self-report data both on drinking problems and on recent use of alcohol from a sample of drivers arrested for drunken driving. Their findings show low but statistically significant correlations between blood-alcohol concentration levels at the time of the arrest and the self-report data. In a much larger study (Sobell et al. 1979), more than 700 alcoholic subjects were evaluated at monthly intervals following treatment. They were asked to provide self-reports of their alcohol consumption during the 48 hours preceding the interview (including the time of the subject's last drink, if any), and were also administered a breath test. The results showed that when subjects had *not* been drinking (negative breath analysis), their self-reports were entirely valid. All subjects in this category said they had not been drinking. However, when subjects had been drinking, their self-reports were often discrepant with their blood-alcohol levels; the patients usually underreported their consumption. When subjects had been drinking, self-report data were consistent with blood-alcohol readings in 44 to 55 percent of all cases tested, depending on the subpopulation group.

Finally, Babor and Mendelson (1979) shed further light on the relationship between self-report data and actual drinking behavior. This paper describes two studies: In the first, 34 volunteer male drinkers were given access to alcohol continuously over a 20-day period; they lived in a research ward setting. Subjects also filled out several self-report measures describing their drinking rate in their normal environments. For most subjects, daily consumption in the ward did not differ significantly from their reported previous consumption. Correlations between a variety of self-report indexes and alcohol consumption in the ward setting showed, generally, that individuals who report heavy consumption of alcohol, and who label themselves heavy drinkers, are likely to be heavy drinkers in situations where actual consumption of alcohol is free to vary over a period of time.

In the second study, 16 regular bar patrons were observed (with their permission) in a tavern setting over a period of 6 weeks (2 days of observation per week). At a later date, all subjects completed the MAST and responded to additional questions about the amount of drinking in both tavern and nontavern settings. Scores on the MAST ranged from 0 to 47, with a mean of 6.1; six subjects in the sample would be classified as alcoholic on the basis of the MAST scoring rules. When MAST scores were correlated with number of drinks consumed and frequency of drinking episodes in the tavern setting, the coefficients were statistically significant—$r = 0.46$ and 0.45 for each measure respectively, $p < 0.05$)—but accounted for less than 25 percent of the overall variance. It is unfortunate that a more precise self-report measure of the quantity and frequency of consumption was not included for this sample. The authors conclude that "commonly used self-report drinking measures are highly effective in differentiating drinkers in terms of more objective indicators of drinking behavior."

Conclusions

The review of the literature generally supports the utility of self-report data in the assessment of drinking behavior. Studies show that the test-retest reliability of such information, obtained from both normal and problem drinkers, is generally high in terms of acceptable scientific criteria. Agreement between reports from alcoholics and collateral sources is also quite good, particularly for the more global indexes of consumption rates. Measures of concurrent validity, in which a direct comparison is made between self-reports of drinking and objective measures of consumption and intoxication (direct observations of drinking, blood-alcohol tests) show the weakest correlations (especially if the subject is asked to provide the self-report shortly after drinking). In most cases, the accuracy of retrospective self-report data deteriorates when subjects are asked to provide specific detailed records of consumption, as compared with more global drinking categories. Similarly, validity is high when subjects are either abstinent or drinking in an uncontrolled manner; accuracy decreases when the drinking varies between these two extremes.

More research is needed, however, to further clarify factors that may influence the reliability and validity of self-report data concerning addiction. A number of questions remain: For example, although we now have some data concerning the concurrent validity (comparisons of self-report data with objective indexes of recent or current consumption) and discriminant validity (the capacity of self-report measures to differentiate between various kinds of drinkers) of self-report measures, we have relatively little information concerning predictive validity (the ability of these measures to forecast future drinking behavior). There is also considerable need for a direct comparison of self-report measures that differ in format—objective descriptions of drinking behavior, compared with more subjective evaluations of drinking problems. A comparison of data obtained concurrently (self-monitoring of ongoing drinking on a daily basis) with data obtained by retrospective accounts also would provide valuable information. Future studies also should make greater use of self-monitoring procedures (daily drinking diaries); this procedure avoids some of the major problems (memory distortions over time) that hinder the accuracy of retrospective self-reports.

Perhaps the most important principle to consider when evaluating assessment procedures is *construct validity* (Cronbach and Meehl 1955). Rather than comparing test results with an independently derived criterion, the assessment of construct validity analyzes how the measure relates to the theoretical system from which the measure is derived. Any information that sheds light on the nature of the theoretical constructs under consideration, or that explains the conditions affecting the behavior being assessed, contributes to the construct validity of the measure. Construct validity is especially important to the evaluation of self-reports of drinking behavior because of the two conflicting theoretical ideologies concerning the nature of alcohol problems. Consider, for example, the conflicting determinants that might influence an individual's response to the following question: "Please describe your drinking behavior on a typical weekend." If the respondent believes that a response to this question might be used as the basis for a diagnosis of alcoholism, the reply could be subject to distortion (underreporting the amount consumed, for example). Or, if the respondent believes that the interviewer is interested only in obtaining objective data to use when developing a treatment intervention program (or as a pretreatment baseline measure of consumption), the reply may be more veridical. Thus, responses to the same assessment item may vary according to the theoretical model (or system of values) employed by the diagnostician. Future research, investigating the influence of varying theoretical models along with other related factors such as setting (situational context in which the assessment occurs) and set (the subject's own expectations concerning the assessment procedure), will provide significant data regarding the construct validity of self-report measures of drinking behavior.

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BIOCHEMICAL ALTERNATIVES TO THE DRINKING HISTORY*

Spencer Shaw

Introduction

The detection of alcoholism, as well as the evaluation of its treatment, has been greatly hampered by the lack of objective tests to assess alcohol consumption. Techniques that utilize patient questionnaires and interviews, job observation, and family interviews require either full cooperation from patients or extensive observations by diagnosticians. Such techniques are costly and subject to error.

Levels of serum enzymes, such as gamma glutamyl transpeptidase (GGTP), however, have been reported to be elevated in alcoholics, and the elevations have been related to the severity of liver damage in alcoholics (Wu et al. 1976). But such elevations are also observed in patients with liver disease and with other diseases unrelated to alcohol (Whitfield et al. 1972; Rutenberg et al. 1963). Thus, increases are not always specifically indicative of alcohol consumption.

Determinations of alcohol in the blood or breath also have been used to confirm alcohol abuse; however, one study found alcohol in the blood of only a minority of heavy drinkers or outpatients with liver injury related to alcohol ingestion (Hamlyn et al. 1975). Furthermore, the measurement of blood or breath alcohol content cannot be used to differentiate occasional alcohol use from its abuse, or to measure alcohol consumption.

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* This work was supported by the Medical Research Service of the Veterans Administration and by U.S. Public Health Service grants AA 03508, AA 00224, and AM 12511.

Recently, the level of the plasma amino acid α-amino-n-butyric acid (AANB) has been found to be increased following chronic ethanol consumption (Shaw and Lieber 1978*a*) and has been suggested as a biochemical marker for heavy drinking. This paper discusses the respective and combined uses of AANB and GGTP evaluations as biochemical alternatives to taking a drinking history.

The Mechanism of Increased Plasma AANB After Chronic Alcohol Consumption

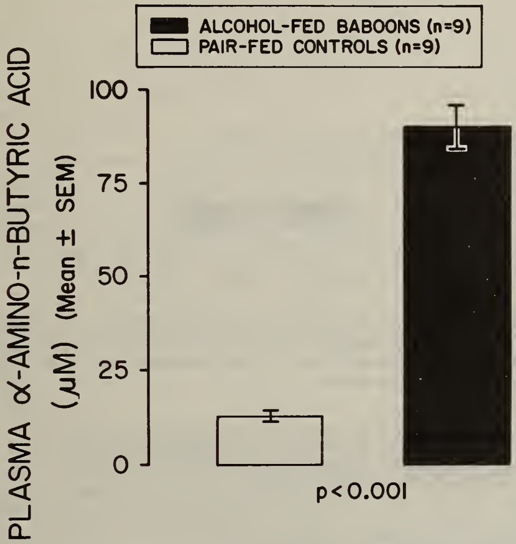
Increased AANB after chronic alcohol consumption was first observed in baboons. When these animals were fed alcohol as 50 percent of total calories with an adequate diet, characteristic abnormalities of plasma amino acids developed, including a six- to sevenfold increase in plasma AANB levels (figure 1). This change was produced after chronic, but not acute, alcohol consumption (Shaw and Lieber 1978*a*). The increase did not depend on the presence of alcohol in the blood and was of equal magnitude in baboons with only steatosis as well as in those with varying degrees of alcoholic hepatitis and fibrosis. Furthermore, the increase occurred gradually during periods of weeks to months. Thus, the change reflected chronic rather than acute alcohol consumption, and was independent of the relatively moderate degree of liver injury.

Plasma AANB can also be increased by metabolic or dietary abnormalities. To investigate whether AANB can be increased under controlled dietary conditions, ethanol was given (2 to 4g/kg/d), in addition to a basal 2,000 kcal diet, to human volunteers on a metabolic ward. AANB progressively increased, with a twofold rise after 2 to 4 weeks (figure 2) (Shaw and Lieber 1978*a*). To determine whether these changes could be due to an imbalance in the source of dietary calories, the volunteers were given calorically equivalent fat or carbohydrate in place of ethanol; no changes in AANB occurred. Thus, the increase in AANB was due to a direct effect of ethanol rather than to dietary imbalance.

Further studies were conducted in the rat and baboon to ascertain the source of increased AANB after alcohol consumption. Compared to pair-fed controls, alcohol-fed rats had a sixfold increase in hepatic AANB and a threefold increase in plasma

AANB (Shaw and Lieber 1978*b*). The increase in gradient from liver to plasma suggested enhanced hepatic production. This

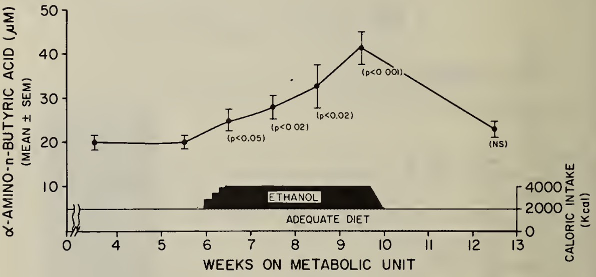
Figure 1. Increased Plasma α–Amino–n–Butyric Acid After Chronic Alcohol Consumption in the Baboon



Animals were fed alcohol as 50 percent of total calories along with an adequate diet for 1 to 4 years.

finding was verified by measuring AANB production in liver slices. Following an overnight fast, AANB production was increased two- to threefold in livers of alcohol-fed animals when compared with controls. Splanchnic output of AANB was determined in baboons chronically fed alcohol (Shaw and Lieber 1978*b*). Following an overnight fast, alcohol-fed animals exhibited splanchnic production of AANB, as compared with pair-fed controls in which there was slight AANB consumption. Thus, the increased plasma AANB in

Figure 2. Progressive Increase in Plasma AANB in Volunteers Studied Under Metabolic Ward Conditions



Ethanol was given as a dose of 2 to 4 g/kg/day, or up to 50 percent of total calories. Reprinted with permission, from Shaw, S. and Lieber, C.S. in *Gastroenterology,* 74:677. Copyright 1978 by The American Gastroenterology Association.

alcoholics can be explained by enhanced hepatic production.

AANB can also be increased in the plasma of patients with severe abnormalities of carbohydrate metabolism, such as diabetic ketoacidosis (Swenseid et al. 1967) and ketogenic diets severely restricted in carbohydrate content (Felig et al. 1970). Such cases, however, do not often present diagnostic problems.

The Mechanism of Increased GGTP After Alcohol Consumption

GGTP is frequently elevated in the blood of alcoholics (Rosalki et al. 1970; Rollason et al. 1972; VanWaes and Lieber 1977) and thus has been proposed as a biochemical marker for alcohol consumption. The mechanism by which alcohol consumption produces an increase in GGTP, however, is controversial. Experimental studies in rats receiving alcohol as percent of total calories have revealed increased GGTP activity in plasma and liver (Ishii et al. 1976; Teschke et al. 1977). Furthermore, the increases in hepatic GGTP were attributed primarily to increases in the microsomal fraction. These observations were consistent with previous findings that alcohol is known to induce liver microsomes (Ishii et al. 1973). Similarly, drugs such as phenobarbital which induce hepatic microsomes, cause an increase in hepatic GGTP in the rat (Iden et al. 1971). In humans, chronic ingestion of phenobarbital and phenytoin (for epilepsy) produces an increase in plasma GGTP (Rosalki et al. 1971).

Morland et al. (1977) suggested that the observed increase in hepatic GGTP after chronic alcohol consumption in the rat was due to differences in carbohydrate content of the alcohol-containing and control diets. Recently, however, studies in rats and humans revealed that diets with ethanol produced increases in GGTP but diets of identical carbohydrate content, substituting fat for ethanol, did not (Shaw and Lieber 1979). Plasma GGTP increased in rats and humans, following doses of ethanol that produced no liver damage other than steatosis. Furthermore, in humans the increases occurred despite no significant changes in serum glutamic oxaloacetic transaminase (SGOT) or glutamic dehydrogenase (GDH) activities, which are elevated in the presence of hepatic inflammation and necrosis (VanWaes and Lieber 1977). Thus, the increase in hepatic GGTP after ethanol consumption in rats was due to microsomal induction, rather than to reduced dietary carbohydrate or nonspecific liver damage. This induction may explain, at least in part, the increased plasma GGTP of alcoholics. Liver damage, of any etiology, however, could further increase GGTP in plasma, and thus could produce false positive tests if an elevated GGTP were used as the only criterion for assessing chronic heavy alcohol consumption.

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Use of GGTP and AANB to Detect Patterns of Heavy Drinking

Investigations in humans confirmed that AANB levels were increased by chronic, but not acute, alcohol consumption (Shaw et al. 1976). However, the increases in AANB due to alcohol can be at least partly offset by a decrease resulting from the dietary protein deficiency commonly present in the alcoholic. To correct for nutritional factors, the level of AANB was therefore expressed relative to branched-chain amino acids, used as markers of dietary protein intake. For convenience, leucine was selected, but similar results were obtained with valine and isoleucine. In humans, the plasma AANB level relative to leucine was found to be increased in the majority of alcoholics, regardless of their nutritional status or the degree of liver injury, except in cases of severe hepatic decompensation or ketoacidosis (Shaw et al. 1976). This increase was reversible following cessation of drinking, persisted for at least several days, did not require the presence of alcohol, and was absent in nonalcoholics with liver disease of viral origin. Furthermore, the usefulness of measuring the plasma AANB level, relative to leucine, was enhanced by the simultaneous measurement of GGTP. Using this combined approach detected a majority (at least 80 percent) of both ambulatory as well as hospitalized alcoholics (Shaw et al. 1978). Thus, the plasma AANB level (corrected for nutritional status), in conjunction with GGTP, provides a biochemical test of recent heavy drinking.

By establishing an early diagnosis, one can recognize alcoholism prior to the social or physical disintegration of the patient, and the outcome of treatment instituted at an early reversible stage can thereby be improved.

Use of AANB and GGTP to Assess Success of Alcoholism Treatment and Relapse

Mean red blood cell volume (MCV), GGTP, and AANB have each been proposed as tests for the assessment of abstinence or relapse following treatment for alcoholism. To evaluate the usefulness of these respective tests for assessing success of alcoholism treatment as well as to detect relapses, we measured MCV, GGTP, and AANB in two different populations receiving treatment for alcoholism—at the Bronx (N.Y.) Veterans Administration (VA) medical center and at Raleigh Hills hospital (Denver) (Shaw et al. 1979). We assessed changes in blood tests during withdrawal from alcohol, during abstinent period, and following relapse of drinking during outpatient followup.

At the VA medical center 77 alcoholics seen for treatment of withdrawal from alcohol or for medical complications of alcoholism were studied. Each received at least 3 weeks of inpatient treatment, and was followed as an outpatient for up to 2 years. At the Raleigh Hills hospital, 168 patients seen and treated for alcoholism were also studied. All received 3 weeks of inpatient treatment and were followed monthly as outpatients for up to 3 months. All patients had been actively drinking within 1 to 2 days before admission. Fifty subjects, including 45 nonalcoholics and 5 alcoholics in remission (studied on a metabolic ward), served as a control group. The criteria of remission and relapse follow:

> *Remission*: No clinical evidence or history of drinking; absence of ethanol in all blood samples.
>
> *Drinking*: History of resumed drinking ($<$ 1 pint 86-proof beverage or equivalent per day); ethanol in any blood sample ($<$ 100mg/dl).
>
> *Heavy Drinking*: History of ethanol consumption ($<$ 1 pint 86-proof beverage or equivalent per day; ethanol in any blood sample $>$ 100mg/dl); evidence of alcohol-related withdrawal or clinical deterioration due to alcoholism.

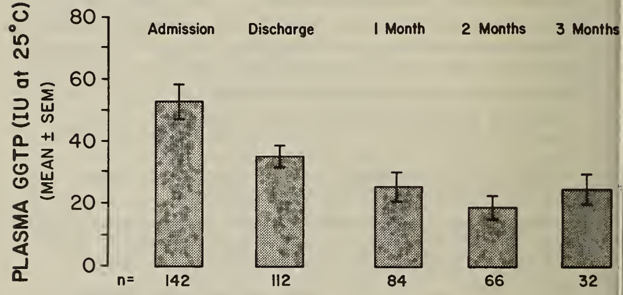
MCV, GGTP, and AANB values on admission, discharge, and during followup in patients in remission were measured. Differences were assessed by paired Student's t-test. The effects of relapse on MCV, GGTP, and AANB were studied for patients at the VA center. Increases above discharge values were calculated for each of these tests, in each subject, and compared to increases observed in a control population. Values exceeding 95 percent of the variability of the control population were considered abnormal. All sample analysis was carried out in a blind fashion.

Among the 77 VA patients treated for alcoholism, 33 remained in remission; 11 resumed drinking; and 33 resumed heavy drinking during the 2-year followup. Among the 168 patients at Raleigh Hills, 155 remained in remission during the 3-month followup.

The effects of withdrawal from alcohol and prolonged remission on MCV, GGTP, and AANB were evaluated in the 33 VA patients and 155 Raleigh Hills patients who remained in remission during followup. MCV did not change in either group of patients following admission and withdrawal from alcohol. In contrast, AANB and GGTP each decreased significantly, to approximately 50 percent of admission values in both groups of subjects during the periods of withdrawal and remission (figures 3, 4, and 5). Mean GGTP values among VA patients decreased from 124.1 international units on admission, to 90.2 on discharge, and to 71.1 during followup.

Raleigh Hills patients had GGTP values of one-half to one-third of those of VA patients during comparable time periods.

Figure 3. **GGTP in Raleigh Hills Hospital (Denver) Patients Following Treatment for Alcoholism**



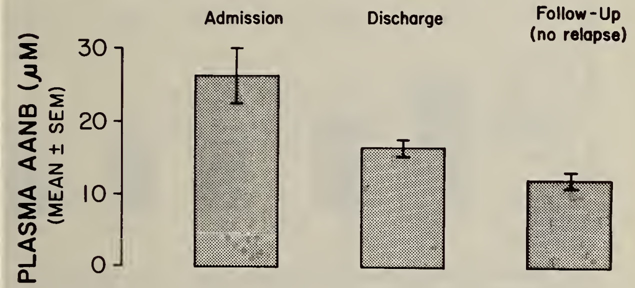
GGTP decreased progressively following admission for inpatient treatment of alcoholism, as well as during outpatient followup (all p<001). Reprinted with permission, from Shaw et al. in *Alcoholism: Clinical and Experimental Research,* 3:297-301. Copyright 1979 by Grune and Stratton.

The effects of relapse on GGTP, MCV, and AANB were evaluated in the 77 VA patients; there were 33 remissions, 11 relapses to "drinking"; and 33 relapses to "heavy drinking" (figure 6). MCV increased above control levels in 5 of the heavy drinkers, in none of the drinkers, and in 2 of the patients in remission. GGTP increased above control levels in 15 heavy drinkers, in 5 drinkers, and in 3 remissions. AANB increased above control levels in 19 heavy drinkers, in 3 drinkers, and in only one remission.

Twenty-six of the 33 patients who resumed heavy drinking had elevated GGTP or AANB levels. Six of the drinkers had such increases and only 4 of 33 patients in remission had increased values in either test.

The results of this study demonstrate that measuring plasma AANB and GGTP levels is useful in assessing both withdrawal from heavy ethanol consumption and remission following treatment for alcoholism. By contrast, MCV was not useful for the documentation of either abstinence or relapse. The combined measurements of AANB and GGTP allow for the detection of an overwhelming majority (80 percent) of patients who relapse, with a tolerable rate of false positive results (about 10 percent).

Figure 4. Decrease in AANB, Following Treatment for Alcoholism Among VA Medical Center Patients

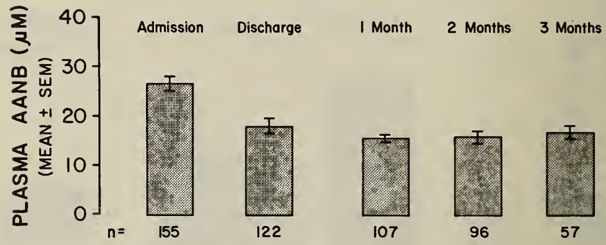


AANB values were significantly lower at the time of hospital discharge and during outpatient followup as compared with admission values (p<.001). Reprinted with permission, from Shaw et al. in *Alcoholism: Clinical and Experimental Research,* 3:297-301. Copyright 1979 by Grune and Stratton.

Summary

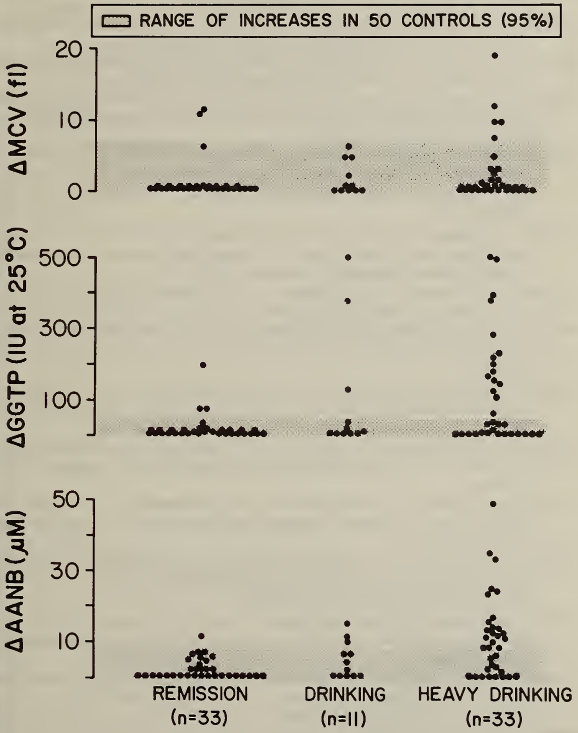
Biochemical tests can provide a useful alternative to the drinking history. Plasma AANB and GGTP levels are increased after alcohol consumption by different mechanisms and may complement each other as tests for heavy drinking. MCV was not useful in this regard. AANB and GGTP measurements can be used to detect relapses or abstinence following treatment for alcoholism, and can thus be used as a guide for patient management, as well as an objective means for comparing different treatment modalities.

Figure 5. **Decrease in AANB, Following Treatment for Alcoholism in Raleigh Hills Hospital (Denver) Patients**



AANB values were similar to those observed among VA hospital patients and were significantly lower on discharge and during followup, as compared with admission values (all p<.001). Reprinted with permission, from Shaw et al. in *Alcoholism: Clinical and Experimental Research*, 3:297-301. Copyright 1979 by Grune and Stratton.

Figure 6. Increases in MCV, GGTP, and AANB (Above Discharge Values) in VA Medical Center Patients During Outpatient Followup



Among patients who relapsed a majority had increased AANB or GGTP, but not increased MCV above that of a control group. Reprinted with permission, from Shaw et al. in *Alcoholism: Clinical and Experimental Research,* 3:297-301. Copyright 1979 by Grune and Stratton.

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DISCUSSION OF PAPERS BY PATTISON, MARLATT, AND SHAW

Thomas F. Babor

These papers do a nice job of illustrating the problems and prospects of quantification in the evaluation of the alcoholic. Implicit in the problem of quantification is the problem of definition. What is the nature of alcoholism? Who shall be called an alcoholic? Since the early Middle Ages, when the scholastic philosophers were attacked for their basically illogical form of dogmatism, the empirical tradition has rejected what has come to be known as the "nominalist" fallacy; that is, that because something can be described and labeled, it exists as a pure entity. This conflict is still with us, both in clinical practice and in the popular mythology, and it must be dealt with.

Many years ago, E.M. Jellinek came to the conclusion that alcoholism was not a specific but a generic term, that the various species have only two elements in common (drinking and damage) and that the genus is too broad to permit specific and meaningful questions. I think it is clear from Mansell Pattison's paper that the NCA criteria were not put through the wringer merely because they resemble a laundry list. The fact is that they are inadequate to describe and diagnose a phenomenon that by most current evidence seems to be a multidimensional, heterogeneous syndrome with multiple etiologies. Unless we are successful in finding an empirical basis for defining and naming these species, and the extent to which individuals diagnosed as alcoholic vary along various dimensions of these species, we will continue to be restricted in our search for reliable and valid diagnostic indicators of both problem drinking and alcohol-related damage.

Each of these papers implies the need to emphasize the multivariate nature of both conceptualization and assessment. They also indicate that new quantification procedures have been developed and that these advances in evaluation technology can be profitably applied to the study of alcoholism. These developments include advances in psychometrics, self-report measurement, biological indicators, multivariate statistical analysis, behavioral description, and the technology of monitoring alcohol consumption.

Alan Marlatt has emphasized the need to improve and standardize the technology of the self-report. When we compare his paper with Spencer Shaw's, we might retitle the latter's paper "Biological Adjuncts to the Drinking History," implying that these procedures should be looked at as complementary methods for assessment and diagnosis. By looking at relations among various kinds of indicators we may get some notion of how alcoholism is patterned and how we might go about differentiating among types and degrees of alcohol dependence.

Finally, I think the papers indicate the state of the art with respect to problems in definition, diagnosis, and quantification. Some would characterize this state as one of confusion. I would see it rather as a period of healthy skepticism—a period when many individuals in the field are attempting to find new explanations for old phenomena, new answers to old questions. We may be moving toward a more probabilistic model of alcoholism, one in which, given a certain number of risk factors and objective indicators of intoxication, the probability could be said to increase that such and such an individual will develop alcohol dependence and additional physical disabilities. Thus, as the research discussed in these papers suggests, it may be important to pay much greater attention to differences than to commonalities among alcoholics.

SESSION II: ALCOHOLISM AND PSYCHOPATHOLOGY

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DEPRESSION AND ALCOHOLISM*

Remi J. Cadoret

Depression and alcoholism are two very common psychiatric conditions. In clinical settings such as detoxification centers, hospital emergency rooms, and psychiatric inpatient and outpatient services, the association of depression and alcoholism is striking. Estimates of the incidence of depression in alcoholics range from about 5 to 60 percent. This paper reviews some of the findings relevant to this association and adds an additional sample to the small number of studies that have already examined the association.

Depression in alcoholic individuals takes several forms, as demonstrated by Winokur and coworkers (1974) who subdivided a sample of 259 alcoholics into two classes of depressives, using the concept of primary and secondary psychiatric conditions developed at Washington University in St. Louis. "Primary" refers to a psychiatric condition that either exists alone or, if another condition is present, started earlier in life than the second condition. "Secondary" refers to a psychiatric condition that began later than the primary condition. Using this scheme with 259 alcoholics, Winokur et al. (1974) reported the breakdown shown in figure 1. A major finding was the preponderance of women alcoholics with primary depression; there were 26 women and only 5 males. These primary depressed women also had a higher incidence of relatives reported having affective disorders.

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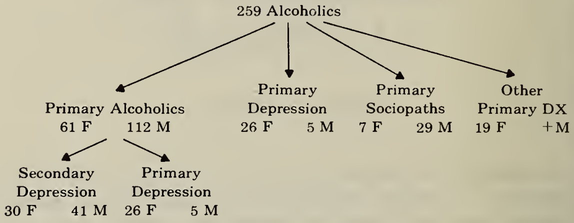
* The author wishes to express thanks to Dr. Alfred Aflatooni for carrying out much of the study reported in this paper, and to Ms. Carol North for technical assistance in analyzing the data.

Depression, current or past, was the most common psychiatric condition reported by these alcoholic patients: 102 out of 259 (39 percent) had depressions. In the depressives, the most common type of affective disorder was a secondary depression. This condition occurred in 71 of the 173 primary alcoholics (41 percent) (Cadoret and Winokur, 1974).

Figure 1. Primary and Secondary Diagnoses of Depression in 259 Hospitalized Alcoholics



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Male and female secondary depressives showed a very significant difference in time of onset of their depressive symptoms, as shown in table 1. More than 10 years elapsed between the onset of alcoholism and depression in a large proportion of the male depressives; in most of the females, the depressions started less than 10 years after the onset of alcoholism.

In comparing depressives with nondepressives, several clinically important features were found to be associated with depression. These differences are shown for males in table 2. Depressive males had more multiple suicidal attempts and these attempts tended to be more medically serious. The drinking pattern of depressive males was more likely to be of the "binge" type.

Somewhat similar clinical differences were found for female secondary depressives, as shown in table 3. More evidence regarding periodicity of drinking was evident in the increased abstinent periods in the female depressives. Again, there was evidence of an association of suicidal behavior with both secondary and primary depression.

Table 1. Time Between Onset of Alcoholism and Development of Secondary Depression

Time Interval (years)	Males		Females	
	No.	Percent	No.	Percent
1-2	4	13.8	7	36.7
3-4	4	13.8	4	21.1
5-6	3	10.3	0	0
7-8	0	0	4	21.1
9-10	0	0	1	5.3
> 10	18	62.1	3	15.8
Total	29	100.0	19	100.0

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There is little evidence from these data of a familial factor in secondary depression: In nondepressed primary male alcoholics, 6 percent of first-degree relatives (parents and siblings) are reported as having affective disorders, compared with 11 percent of the relatives of depressed males. This difference is not significant. In primary alcoholic females with secondary depression, 8 percent of the first-degree relatives have affective disorders, in comparison with 7 percent of the relatives of nondepressed patients. Again, this difference is not significant. However, Schuckit et al. (1969) showed that 17 percent of first-degree relatives of alcoholic primary depressed females have affective disorders, a difference that is statistically significant when compared with the pooled rate in relatives of primary alcoholic females.

Thus, the division of depression in alcoholics along the lines dictated by the concept of primary and secondary conditions leads to the discovery of important clinical and familial differences. The finding of more episodic or periodic drinking in the secondary depressives is reminiscent of the findings of Amark (1951), who reported more episodes of drinking in cyclothymic alcoholics.

The other important clinical feature is the association of suicidal behavior with depression. The finding of suicide attempts of depressive alcoholics is of potential importance in the practical clinical management of such patients.

Table 2. Alcoholic and Psychiatric Symptoms in Male Alcoholics With and Without Depressive Syndrome

Symptom	Without Depression	With Secondary Depression
Alcoholic paranoia	23%	2%[a]
Benders	58%	78%[b]
Two or more suicide attempts	3%	24%[a]
Number of serious suicide attempts (of those made)	(2/12)[c] 17%	(6/17)[c] 35%
No suicidal ideation or attempts	68%	20%[a]

[a] Significant difference at 1% level.

[b] Significant difference at 5% level.

[c] Numerator = number of medically or psychiatrically serious attempts; denominator = total number of suicide attempts in the group.

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Unfortunately, no study has been made of the depressions occurring in the sociopathic alcoholics of the Winokur study. Depression is common in sociopaths at psychiatric outpatient clinics. For example, in an emergency room study in St. Louis, Robins et al. (1977) found that approximately 25 percent of the alcoholics had a diagnosis of antisocial personality. Thus, a sample of depressed sociopathic alcoholics in a study of secondary depressives, were included and compared with depressed primary alcoholics.

Accordingly, we collected data for a 3-month period at the University of Iowa Alcoholic Treatment Center at Oakdale. Each subject received a structured psychiatric interview, designed to detect affective disorder (mania and depression), anxiety, obsessional neurosis, phobic neurosis, hysteric neurosis, schizophrenia, and antisocial personality. All admissions for alcohol detoxification

Table 3. Alcoholic and Psychiatric Symptoms in Female Alcoholics With and Without Depressive Syndrome

Symptom	Without Depression N = 31	With 2° Depression N = 30	With 1° Depression N = 26
Never abstinent	55%	20%[b]	8%
Abstinent 3 months or longer	35%	77%[d]	92%
Median age at diagnosis of alcoholism	30-35	25-29	40-44[a]
Number of serious suicide attempts	1/5 (20%)	3/13 (23%)	4/8 (50%)
Percentage of individuals making 2 or more suicide attempts	10%	23%	35%
Percentage of patients without suicidal ideation or attempts	61%	33%	23%[c]

[a] Significant difference at 5% level in primary versus secondary depressives.

[b] Significant difference at 5% level in secondary depressives without depression.

[c] Significant difference at 5% level in primary depressives versus those without depression.

[d] Significant difference at 1% level in secondary depressives versus those without depression.

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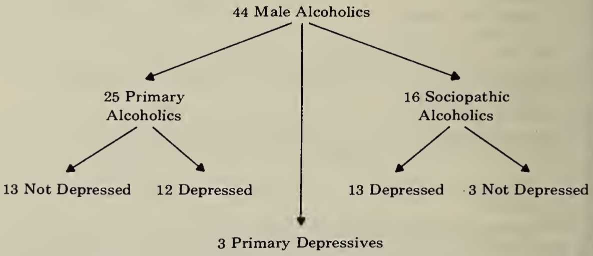
during a 3-month period were eligible. Of 67 such admissions, 45 were interviewed; the remainder left the hospital before the interview, which was usually held on day 2 or 3 after admission. Forty-four of the admissions were male and one was female; the 44 male subjects were used for the present study. All of those in the study met Feighner (Feighner et al. 1972) criteria for alcoholism.

Secondary depression was defined as an affective episode characterized by low mood plus four depressive symptoms from the Feighner list and lasting at least 2 weeks. Antisocial personality was also diagnosed using Feighner criteria. For analyses, definite plus probable diagnoses of antisocial personality were combined.

Figure 2 shows the breakdown of the 44 male alcoholics into primary and sociopathic alcoholics, and the number of each who reported symptoms of secondary depression.

Figure 2. Primary and Secondary Diagnoses in 44 Male Alcoholics



Three primary depressives (7 percent) were found; 16 (36 percent) sociopathic alcoholics and 25 (57 percent) primary alcoholics comprised the remainder of the sample. A total of 25 (57 percent) secondary depressives was found. Although the incidence of depression appears higher in the sociopaths, the difference in depression incidence is not significant between sociopaths and primary alcoholics. The number of secondary depressions present at the time of admission was 15 (34 percent), so the rather high rate of secondary depressions was likely attributable to individuals with past or present depressions.

The number of years from onset of alcoholism to onset of secondary depression is shown in table 4.

Table 4. Time From Onset of Alcoholism to Onset of First Depression in Primary and Sociopathic Alcoholics

Years	Primary Alcoholics	Sociopathic Alcoholics
0–2	1	5
3–5	1	2
6–9	0	1
10+	7	1
Unknown	3	4

Here a familiar pattern emerges. These primary alcoholics showed the same delay in development of depression as did those in the St. Louis study (table 1).

In contrast, sociopathic alcoholics showed little evidence of such a delay. In sociopaths it appears that the onsets of depression and alcoholism are almost simultaneous, suggesting that the depression is part of the sociopathic condition. The difference in patterns of the primary and sociopathic alcoholics is significant.

As might be predicted from the results of the St. Louis study, suicide attempts were also found. Table 5 shows the rates for each alcoholic subtype.

Table 5. Suicide Attempts and Depression

	With Depression	Without Depression
Primary alcoholics	0/12 (0%)	1/13 (8%)
Sociopathic alcoholics	4/13 (31%)	0/4 (0%)
Primary depressives	3/3 (100%)	-
Total	7/27 (26%)	1/17 (6%)

Although the difference in rates between depressed and nondepressed individuals for each subtype is not significant, the suicide attempt rates do occur as expected, and the difference between the primary alcoholics and the primary depressives in this respect is significant, despite the small sample sizes. There is no significant difference between the incidence of binge drinking in the depressives (33 percent) and the nondepressives (25 percent).

Attempts were made to search for reasons for secondary depression in the sample of 44 alcoholics. Serious social losses, including marital separation, divorce, and losses of significant others through death, have been cited as precursors of suicide in alcoholics (Murphy and Robins 1967; Murphy et al. 1979). We looked for similar factors associated with secondary depression in these patients (although there is some question as to whether depression is a necessary or sufficient antecedent of suicide in alcoholics). Part of the routine admission questionnaire asked about such personal losses in the past year. Of currently depressed individuals, we found that 73 percent reported such a loss, compared with 43 percent of the nondepressed individuals. This tabulation did not include primary depressives, none of whom was depressed at the time of admission. Although the difference is not statistically significant, it is consistent with reported findings on stressful life events and the studies of life events preceding suicide in alcoholics (Murphy and Robins 1967; Murphy et al. 1979).

This study of 44 alcoholics presents evidence that secondary depression is a common complication of alcoholism, at least among patients admitted to detoxification treatment units. The rate of secondary depression found here is similar to those reported in the literature; for example, the Woodruff et al. (1973) report of 55 percent of alcoholic outpatients secondarily depressed, the Robins et al. (1977) finding of affective disorder in 33 percent of 112 alcoholics in an emergency room setting, and the Weissman et al. (1977) report of 59 percent of 61 alcoholic outpatients having secondary depression. One study is not in this range of rates; Fowler et al. (1977) reported finding only 5 percent of the alcoholics secondarily depressed in a hospitalized Veterans Administration sample of alcoholics. The reasons for this variance are not at all clear, but factors such as depressive criteria and differing samples are undoubtedly important.

The finding that secondary depression in sociopathic alcoholics seems somewhat different clinically from secondary depression in primary alcoholics suggests that future studies of secondary depression in alcoholics should account for this diagnostic factor. It would be especially important if some sociopathic alcoholics with depression were more prone to suicide attempts and completed suicides. Followup studies initiated in detoxification centers and continued over a period of time would help answer this important question.

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ALCOHOLISM AND THE "ALCOHOLIC" PERSONALITY

Raymond M. Costello

The epistemology of personality as a theoretical construct has been intriguing. From the ancient concept of humors, to the structural and topographic theories of Freud, and now aided by the immense capabilities of the electronic computer, the limits and validity of theory contract and expand with each new discovery. However, discoveries in the area of alcoholism and personality have been few. Personality descriptions of the alcoholic tend to be gross oversimplifications, as one (dependency conflict) or few concepts are put forward to encompass one of the most damaging and complicated of human conditions. For whatever reasons the distortion occurred, the current social, economic, and professional climate favors intense investigation in the area. This conference has been organized to provide an updated summary of research and theory in many areas relating to the alcoholic, with a description of the implications of scientific evaluation and treatment of such individuals. In the domain of questionnaire-oriented personality research, this paper discusses discoveries sufficiently basic to warrant the status of "organizing principles."

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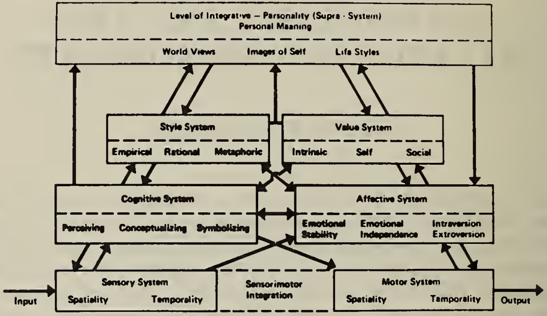
What Is Personality?

Personality, of course, is not simply whatever is measured by the Minnesota Multiphasic Personality Inventory (MMPI) or any other such static measure. It is a dynamic and complex system, as complicated as any other human system—central nervous, cardiovascular, or respiratory. Figure 1, reproduced from the work of Wardell and Royce (1978), illustrates the complexity of this system.

Figure 1. Integrated Personality System



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The sensory, motor, cognitive, affective, apprehending style, and social-moral value elements of the system are in flux. The integration within and between subsystems into the suprasystem of personal meaning or consciousness (world view, self-image, life-style) constitutes personality. This paper focuses on the subsystem labeled "Affective" by Wardell, as most of the work with questionnaire measures of personality is located in this subsystem.

Caveats

Some caveats should be introduced before proceeding. First, Tryon (1979) and associates warned that tests have been used as shortcuts to understanding behavioral facts. Scores on tests are transformed from dependent measures of theoretical constructs to independent explanations of subsequent events. The understanding of the causal sequence is illusory when such tautological reasoning is employed. The test used to document the existence of a not-otherwise-observable phenomenon is applied in turn to explain other phenomena. Tryon argues that such tests, properly used as dependent variables, are misused as predictor variables.

Second, the modern trend is to view all personality sybsystems as multivariate. For every "n" dimensions considered elemental, 2^n types of person-classes could be described if the elements are dichotomized (Maxwell 1971). Thus, if Cattell's (Cattell et al. 1970) 16 personality factors were considered elemental, 2^{16} or 65,536 personality categories would be possible in the Affective subsystem.

Third, the press of such numbers will force a consideration of the hierarchical order of constructs. Cattell has dealt with this problem factor analytically and has produced constructs which he labels primary, secondary, and tertiary—from highly specific to very broad.

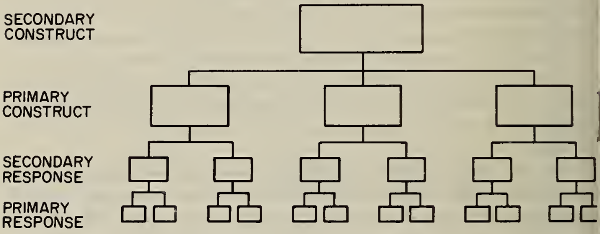
Finally, even if a limited number of elements achieves universal acceptance, the natural distribution of those elements must be determined. Some distributional theory other than the normal might be more representative for the task at hand.

Sources for Review

This section reviews 17 reports on 10 questionnaire tests of personality: the 16 Personality Factor (PF) Test (Costello et al. 1978; Lawlis and Rubin 1971; Nerviano and Gross 1973), the MMPI (Finney et al. 1971; Mogar et al. 1970; Stein et al. 1971), the Inventory of Habits and Attitudes (Haertzen et al. 1969), the Drinking History Questionnaire (Horn and Wanberg 1969; Horn et al. 1974), Adjective Checklists (Jansen and Hoffman 1972; Layden and Smith 1973; Key et al. 1972), the Interpersonal Orientations Form (Key et al. 1972), the California Q Set (Jones 1968), the California Psychological Inventory (Stein et al. 1971; Kurtines et al. 1978), the Loneliness Scale (Nerviano and Gross 1976), and the Differential Personality Inventory (Skinner et al. 1974; Skinner et al. 1976).

In my estimation, consistencies are apparent across these studies, but this congruence has not been appreciated because investigators generally work without a theoretical base. Also, investigators have not consistently referred to a hierarchical construct model such as that shown in figure 2. Indexes at various levels are studied without reference to a nomothetical context. Facts collected are a melange of horizontal, vertical, and crossed findings (within and across constructs) which confuse rather than elucidate.

Figure 2. Hierarchical Model of Responses and Organizing Constructs



Heirarchical Model of Responses and Organizing Constructs

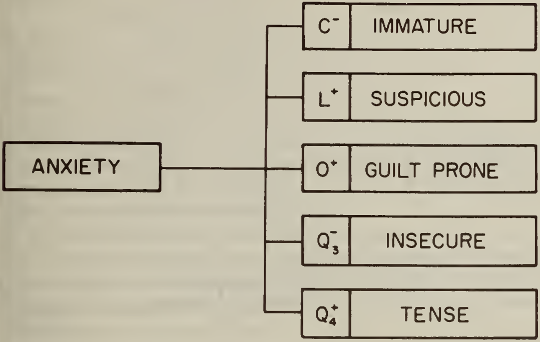
Organizing Principles

At least two dimensions are tapped by "personality" questionnaires. For each dimension, an assumption is made of a "normal" phenomenology and the respondent declares the degree and direction of personal deviation from the normal. The specific content of the items is not essential.

First, the subject is asked to evaluate the phenomenology of "self as an object." In semantic differential terms, this construct is the General Evaluation (good v. bad) dimension. On the MMPI, it is reflected as profile elevation, from general elevation to submerged. On the Drinking History Questionnaire (DHQ), the second-order general severity dimension (Horn and Wanberg 1969) probably best reflects the construct. Cattell and coworkers (1970) recognized this construct as one of the two most important second-order dimensions on the 16PF—Anxiety v. Adjustment. Hierarchically, this anxiety construct is organized as shown in figure 3.

Second, the subject is asked to evaluate the phenomenology of "self in relationship to others." In semantic differential terms, this construct is probably the Activity (active v. passive) dimension. The MMPI probably reflects this measure as elevations on scales 3 (Hy),

Figure 3. Hierarchical Anxiety Model



4 (Pd), and 9 (Ma), as opposed to elevations on scales 2 (D), 7 (Pt), and 0 (Si). On the DHQ, the second-order social benefit dimension (Horn and Wanberg 1969) probably best reflects the construct. Cattell and coworkers (1970) recognized this construct as one of the two most important second-order dimensions on the 16PF, Exvia v. Invia. Hierarchically, the Exvia dimension is organized as shown in figure 4.

Thus, items can be construed to reflect two orthogonal dimensions: A self-as-object axis and a self-in-relationship-to-others axis (figure 5). An example of such a two-dimensional space would consist of rating the degree of emotional control (stability of self-sentiment) from overcontrolled or Rigid (a hypertrophied sense of goodness) to Labile; and the degree of social involvement from Withdrawn (passive) to Activated. Nine personality types can be defined if these dimensions are trichotomized into high, medium, and low. Four types can be described if these dimensions are dichotomized into high and low.

Typologies derived empirically capitalize on sample-specific associations, random, artifactual, and real. The computer has given birth to a new generation of researchers who work in this mode. Axes such as those shown in figure 5 are generated as a result of various statistical procedures employed after using some clustering

Figure 4. Hierarchical Exvia Model

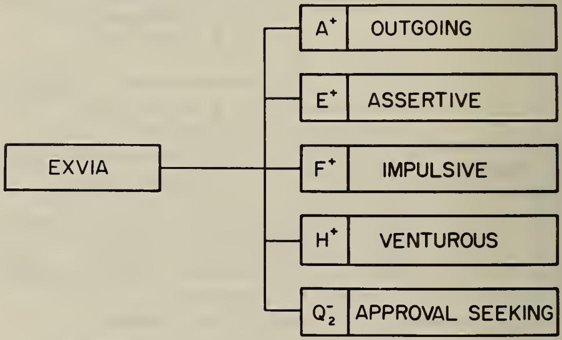
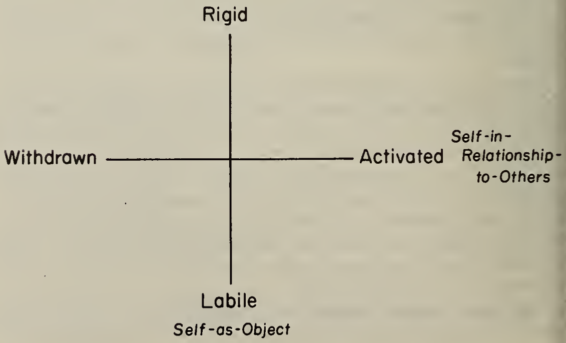


Figure 5. Two-Dimensional Personality Model



technique to establish group membership. These axes frequently are not replicable. With the 16PF, however, there is a fairly broad consensus among researchers that at least two second-order constructs, or redundant primary scale patterns, are present across many different samples. If the computer has not been programed to recognize one or more redundant patterns inherent in the instrument, statistical procedures are likely to assemble an organizational principle or classification rule which mixes up, in a nonreproducible way, basically orthogonal (independent) constructs. This distortion accounts for the shrinkage evident when investigators attempt to replicate their own or another's work.

Also, the complicated statistical procedures used by computer-oriented researchers (for example, Q-type factor analysis followed by multiple discriminant analysis) require an expertise frequently not available to the practicing clinician. Thus, this literature generally seems foreign to the clinician.

Clinicians have been trained and computers can be programmed to recognize syndromes, i.e., redundant patterns of scores. Theory-based typologies can be constructed on the basis of juxtaposition of such score patterns. What follows is a model of such a theory-based typology.

Instructional Model

The two axes shown in figure 5 are operationalized when the test-taker responds to an instrument (in this case, the 16PF) in a psychologically consistent manner. If the individual presents as emotionally labile, the pattern of five anxiety scales will be internally consistent: Scales L, O, and Q_4 will be elevated; scales C and Q_3 will be depressed. (These scales are listed in table 1.) Likewise, a person presenting as socially withdrawn will show an Exvia scale pattern of depression on scales A, E, F, and H and an elevation on Q_2. To test this hypothesis, the 16PF profiles of 150 alcoholics were studied (Costello et al. 1978). Of these, 120 (80 percent) were classifiable. The classification required patients to score outside the normal 4 to 6 stenscore range on four of the five scales, on *either* axis, in a construct-consistent way. This score qualified a subject for placement in a row-marginal or column-marginal cell (cells II, IV, VI, and VIII in figure 6). A patient so scoring on *both* axes was placed in a corner cell (I, III, VII, and IX of figure 6). Subjects who qualified within the normal 4 to 6 stenscore

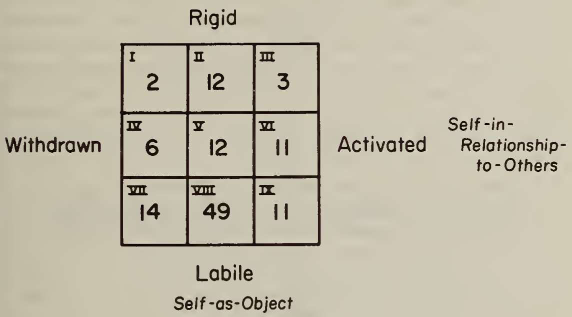
Table 1. Profile Patterns for Nine 16PF Alcoholic Types

		TYPE								
	SCALE	I	II	III	IV	V	VI	VII	VIII	IX
A	Affectothymia	3.5	6.3	6.7	3.3	6.0	7.5	4.2	6.1	8.5
B	Intelligence	2.0	4.5	2.3	5.0	3.7	4.5	4.4	5.0	5.3
C	Ego Strength	7.0	5.8	7.0	4.3	4.5	4.8	2.6	2.3	1.7
E	Dominance	4.0	5.4	7.0	3.2	4.3	6.9	2.4	4.0	5.4
F	Surgency	3.0	3.8	6.0	2.7	4.5	6.3	3.2	4.4	7.0
G	Superego Strength	7.5	6.2	7.3	7.3	6.1	6.9	4.8	5.3	5.4
H	Parmia	3.0	6.1	7.7	1.8	4.9	7.3	2.7	4.1	6.6
I	Premsia	4.0	4.4	4.3	5.3	4.9	4.6	5.4	4.6	5.4
L	Protension	3.5	4.7	4.3	6.7	5.3	6.1	7.9	7.4	7.5
M	Autia	2.5	3.9	4.3	4.3	4.4	5.3	4.4	4.9	5.0
N	Shrewdness	7.0	5.7	4.3	5.5	6.3	5.9	7.6	6.8	5.8
O	Guilt Proneness	3.5	3.8	3.7	6.0	5.7	6.2	8.0	8.0	7.1
Q_1	Radicalism	2.0	2.7	2.3	3.7	3.5	4.6	3.9	4.0	4.4
Q_2	Self-Sufficiency	3.0	3.8	3.3	6.2	4.7	2.8	6.4	4.3	3.1
Q_3	Self-Sentiment	7.5	8.0	6.7	6.5	7.3	7.6	4.6	4.6	4.0
Q_4	Tension	3.5	3.1	4.0	7.0	5.6	6.3	7.9	7.7	7.8

Note: I = Rigid-Withdrawn; II = Rigid; III = Rigid-Activated; IV= Withdrawn; V = Normal; VI = Activated; VII = Labile-Withdrawn; VIII = Labile; IX = Labile-Activated.

range on three of the five primary scales on each construct qualified for placement in the normal cell (V).

Figure 6. Distribution of Alcoholics into Types



I 2	II 12	III 3
IV 6	V 12	VI 11
VII 14	VIII 49	IX 11

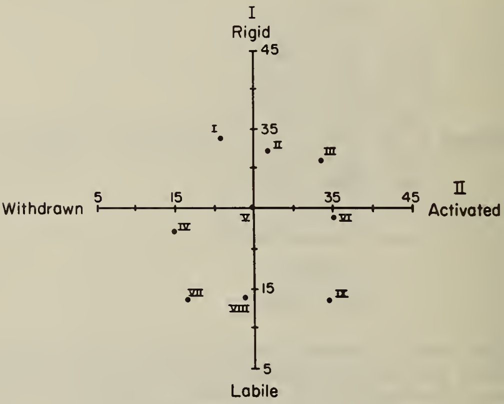
The first finding of interest is the distribution of the 120 subjects into cells or types. Two cells, Rigid-Withdrawn and Rigid-Activated, have very few members, two and three respectively. One cell contains the modal type: Labile has 49 patients, or 41 percent. The remaining cells contain intermediate proportions of cases: Withdrawn, 6; Activated, 11; Labile-Activated, 11; Rigid, 12; Normal, 12; and Labile-Withdrawn, 14.

The statistical distribution of persons on the social axis approximates normality (22 Withdrawn; 73 Normal; 25 Activated), but the distribution of persons on the self-evaluation axis is definitely skewed (74 Labile; 29 Normal; 17 Rigid). These findings are consistent with clinical experience and questionnaire-research findings.

Figure 7 displays the group centroids on the two axes. Although a nonparametric principle was used for classification, the centroids reflect the differential emphasis for types on the two basic dimensions.

The Anxiety and Exvia constructs use 10 of the 16 PF scales. Two-way, univariate analyses of variance were conducted on the other six scales to see if interpretable relationships existed between these scales and the cardinal constructs. No relationships were discovered for scales B (Intelligence), I (Harria v. Premsia), or M (Praxernia v. Autia). Statistically significant main effect relationships with the Anxiety construct were found, however, for scales G (superego strength; F = 7.7, df = 2, 111, $p < .001$), N (naivete v. shrewdness; F = 3.19, df = 2, 111, $p < .05$), and Q_1 (conservatism of temperament v. radicalism; F = 5.5, df = 2, 111, $p < .005$). The 74 patients who characterized themselves as Labile also described themselves as lower (tested *a posteriori* with Duncan's Multiple Range) in superego strength than the other two groups. (5.19 v. 6.53 and 6.66), and as more shrewd than the Rigid groups (6.80 v. 5.59). The Rigid groups described themselves as more conservative than either of the other two groups (2.53 v. 3.97 and 4.04). Thus, high superego strength, naivete, and conservatism of temperament accompany a hypertrophied good self-concept or Rigid emotional

Figure 7. Group Centroids in Two-Dimensional Space



Centroids on the vertical axis were calculated according to the following formula: $30 + C + Q_3 - L - O - Q_4$. Centroids on the horizontal axis were calculated according to the following formula: $10 + A + E + F + H - Q_2$.

control. Table 1 provides summary data on nine of the 16PF profile types.

The 16PF version used in this research was that contained in the Clinical Analysis Questionnaire, CAQ (Delhees and Cattell 1975). The CAQ also comprises a 12-factor pathology supplement somewhat like the MMPI. Subjects' scores on the pathology supplement were used to test for concurrent validity or generalization from the normal personality domain to the clinical symptom domain. Two-way analyses of variance were computed on each pathology scale. Results must be interpreted with caution because cells are confounded by "n" (that is, they contain unequal numbers of subjects), and two cells have little variance because of extremely limited numbers. Furthermore, a multivariate strategy is technically preferred to the repeated univariate analysis. At this preliminary stage of the research, however, the approach is defensible.

The Rigid-Labile dimension correlated significantly with scores on 11 of the 12 pathology scales in the expected directions (D_1: $F = 20.3$, df $= 2, 111$, $p < .001$; D_2: $F = 23.5$, $p < .0001$; D_4: $F = 7.6$, $p < .001$; D_5: $F = 23.8$, $p < .0001$; D_6: $F = 26.5$, $p < .0001$; D_7: $F = 5.9$, $p < .004$; Pa: $F = 3.4$, $p < .04$; pp: $F = 5.7$, $p < .004$; Sc: $F = 6.6$, $p < .002$; As: $F = 12.4$, $p < .0001$; Ps: $F = 12.4$, $p < .0001$). In each case, a linear trend was evident; the groups that characterized themselves as Labile also rated themselves as pathological, and the groups that characterized themselves as Rigid consistently denied pathology. The normal groups were in between. Thus, a powerful general trend (not a specific focus) was discovered. A description of self as object on a Labile-Rigid dimension in the personality domain had a predictable corollary in the symptom domain.

The Withdrawn-Activated dimension correlated significantly with scores on six pathology scales (D_3: $F = 6.2$, df $= 2, 111$, $p < .003$; D_4: $F = 6.9$, $p < .001$; D_7: $F = 5.9$, $p < .004$; Pp: $F = 3.3$, $p < .04$; Sc: $F = 4.0$, $p < .02$; Ps: $F = 5.1$, $p < .007$). In each case, the Normal activation group was in between the other two, and the withdrawn group reported more pathology. Withdrawn subjects described themselves as unwilling to try new things, clumsy in handling things, people-avoidant, timid, inhibited, and retreating from reality.

Only one Anxiety χ Exvia interaction was discovered. This finding may be attributable to chance because of the repeated analyses. On the other hand, subsequent investigators (who have access to more subjects and who can control confounding by cell size) may find more interactions. Table 2 provides summary data on the 12 pathology scales for the nine 16PF types.

An examination of the profile patterns for the nine 16PF types reveals an internal consistency founded on a sound, theoretical basis. It is a complicated but predictable matrix of scores which had not been discovered by investigators working without theory. Although the theory espoused here is simple, drawing on only two constructs, it is nonetheless comprehensive in that much information can be organized with the two principles in question. Whether consistent results will be found when the examination involves domains other than the single-administration questionnaire has not been determined.

A Final Word

In the instructional model just presented, there is great danger of committing the test-trait fallacy which Tryon decried. If individuals are categorized into types, the test scores used in the classification can become reified into causal forces to "explain" other behavioral facts. For example, the corollary findings on the pathology supplement could be attributed to the motive force of the two cardinal constructs drawn from the 16PF. To avoid the test-trait fallacy, such findings must have been seen as evidence of concurrent (rather than predictive) validity, as dependent rather than independent phenomena.

The implication of this advice for clinicians who work with alcoholic patients is to use caution—not to think that we know more about the reasons for our clients' behavior than we really do. We must avoid the simplistic allure of the notion that test scores imply traits. Rather we must monitor the responses of clients to our interventions in the context of a theoretical nomothetic network. By so doing, we can clinically establish the conditions sufficient to produce behavior along a dimension of interest (e.g., social activation). The research cited earlier has provided two axes on which behaviors can be mapped in response to various clinical trials. If we fail to heed Tryon's advice, we are likely to be diverted onto the course of searching for an "alcoholic personality"—a search that has only impeded progress toward more important goals.

The implications for us as personality researchers are twofold. First, we must use the enormous capacity of the computer to test

Table 2. Pathology Scales Patterns for Nine 16PF Alcoholic Types

SCALE		TYPE								
		I	II	III	IV	V	VI	VII	VIII	IX
D_1	Hypochondriasis	6.0	3.9	3.3	6.3	5.9	5.5	8.3	7.7	7.7
D_2	Suicidal Disgust	1.0	3.6	2.3	4.0	4.8	5.9	7.8	7.0	6.7
D_3	Brooding Discontent	3.5	5.5	5.7	3.2	5.3	4.9	3.5	4.9	5.5
D_4	Anxious Depression	6.5	5.2	5.0	7.0	5.9	5.5	8.6	7.4	5.6
D_5	Low-Energy Depression	4.0	4.3	3.7	4.3	4.5	5.7	7.4	7.4	6.3
D_6	Guilt and Resentment	4.5	5.3	5.7	6.8	6.9	7.6	8.1	8.4	7.7
D_7	Bored Depression	5.5	3.9	3.0	5.3	4.5	3.1	7.0	5.6	4.7
Pa	Paranoia	4.5	4.6	5.0	5.3	5.8	3.8	6.4	6.2	5.6
Pp	Psychopathic Deviation	3.0	5.5	6.0	4.7	5.2	5.2	3.5	3.9	5.1
Sc	Schizophrenia	5.5	4.0	4.0	5.8	4.8	4.1	6.7	6.2	4.7
As	Psychasthenia	3.5	3.9	4.3	6.3	5.8	5.2	6.6	6.7	5.7
Ps	General psychosis	2.5	5.8	3.0	7.3	5.3	5.4	8.6	7.2	6.4

Note: I = Rigid-Withdrawn; II = Rigid; III = Rigid-Activated; IV= Withdrawn; V = Normal; VI = Activated; VII = Labile-Withdrawn; VIII = Labile; IX = Labile-Activated.

the limits and validity of our theoretical concepts—not to "go hunting" for unknown quarry. If theoretical constructs are found to have the internal consistency predicted, then the computer should be programmed to recognize this patterning as it scans the primary data. Second, the simplistic appeal of the multiple regression statistic which often produces large multiple correlations, must be tempered if, in the process, test scores are reified into causal forces.

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THE DIAGNOSIS OF ALCOHOLISM AFTER *DSM III* *

Lee N. Robins

Alcohol-Related Diagnoses in *DSM III*

Diagnoses related to the use or abuse of alcohol appear in two sections of the third edition of the *Diagnostic and Statistical Manual (DSM III)* (American Psychiatric Association 1980), under "Organic Mental Disorders" and also under "Substance Abuse Disorders." Under Organic Mental Disorders, as table 1 shows, are seven diagnoses attributed to the use of alcohol: alcohol intoxication, alcohol idiosyncratic intoxication, alcohol amnestic disorder, dementia associated with alcoholism, alcohol withdrawal, alcohol withdrawal delirium, and alcohol hallucinosis. The first two diagnoses do not imply either chronic or prolonged alcohol intake. The other five, however, occur only after excessive alcohol consumption over some period of time.

The diagnoses under Substance Abuse Disorders are listed under the major topic, "alcohol dependence," and subdivided into abuse and dependence. The words "abuse" and "dependence" are used, rather than "probable" and "definite" alcoholism, to emphasize that alcohol is a drug, and that the disorders associated with its excessive use are to be described in terms similar to those used for disorders arising from the intake of other drugs. Alcohol dependence corresponds to what used to be called "alcoholism," and alcohol abuse corresponds to what used to be called "probable alcoholism."

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* This work is supported by grants DA 00013, AA 03539, and AA 03852 from the U.S. Public Health Service.

This paper concentrates on the diagnoses under substance abuse. It explains how to make a diagnosis according to *DSM III*, how the selection of criteria developed, and what problems in alcohol diagnosis remain. Finally, the accuracy and consistency of alcohol diagnoses are compared with those of other psychiatric diagnoses.

Table 1. Diagnoses Related to Alcohol in DSM III

Alcohol Organic Mental Disorders	
303.00	Alcohol Intoxication
291.40	Alcohol Idiosyncratic Intoxication
291.10	Alcohol Amnestic disorder
291.2x	Dementia Associated with Alcoholism
291.80	Alcohol Withdrawal
291.00	Alcohol Withdrawal Delirium
291.30	Alcohol Hallucinosis
Substance Abuse Disorders	
303.9x	Alcohol Dependence
	Alcohol Abuse
	Alcohol Dependence

General Scheme of *DSM III* Regarding Alcohol Abuse and Dependence

In *DSM III*, the descriptions of alcohol abuse and dependence follow the same general pattern as those of other diagnoses in the volume. First, each diagnosis is assigned a number corresponding to the number of the same syndrome as listed in the *International Classification of Diseases (ICD)*, so that the two documents will be compatible. Next, each diagnosis is assigned to an axis. *DSM III* allows coding a subject on five different axes. Alcohol abuse and alcohol dependence fall on axis I, Clinical Psychiatric Syndromes and Other Conditions. Someone assigned a diagnosis of alcohol dependence or abuse can be simultaneously coded on axis II for a personality disorder, on axis III for a physical disorder, on axis IV for psychosocial stress, and on axis V for adaptive functioning in the last year. *DSM III* also permits an individual to be assigned more than one diagnosis on axis I, although some diagnostic combinations are not allowed. However, no other diagnoses on axis I preclude diagnoses of alcohol abuse or dependence.

The text of *DSM III* initially describes the symptoms, subclassifications, associated features, age of onset, complications, predisposing factors, prevalence, sex ratio, and differential diagnosis of Substance Abuse Disorders as a whole. Under alcohol dependence are sections on course, family patterns, and diagnostic criteria; this paper focuses on those criteria.

Diagnostic Criteria

Throughout *DSM III*, diagnostic criteria are listed as groups of symptoms, each group designated by a capital letter. To receive a positive diagnosis, an individual must present at least one symptom from each lettered group: table 2 shows the titles under which alcohol symptoms are grouped.

Table 2. The DSM III Criteria for the Diagnoses of Alcohol Abuse and Dependence

Alcohol Abuse

A. Pattern of pathological alcohol use

B. Impairment in social or occupational functioning due to alcohol use

C. Duration of disturbance at least 1 month

Alcohol Dependence

A. Either A or B above

B. Either tolerance or withdrawal

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For alcohol abuse, group A is Pattern of pathological alcohol use, B is Impairment in social or occupational functioning due to alcohol use, and C is Duration of disturbance for at least 1 month. The C criterion thus distinguishes alcohol abuse from alcohol intoxication, which can arise from a single drinking bout and which can also impair social and occupational function. The C group thus exempts those who merely taste and experiment from receiving a diagnosis of abuser.

For alcohol dependence, group A combines the criteria of groups A and B in alcohol abuse, and category B is either tolerance or withdrawal. Combining A and B of alcohol abuse into a single category in alcohol dependence permits application of the rule that there must be at least one positive symptom in each lettered group of symptoms. Thus, for alcohol dependence, one must have tolerance or withdrawal, and, in addition, *either* a pattern of pathological alcohol use *or* impairment of social or occupational function. A patient need not have both.

Roots of *DSM III* Diagnosis of Alcohol Dependence

The *DSM III* diagnostic system grew out of the Research Diagnostic Criteria or RDC (Spitzer et al. 1975) which, in turn, developed from the Feighner criteria (1972). The RDC were originally developed for the National Institute of Mental Health's ongoing Collaborative Depression Study. During the planning years, two of the members of the discussion group were Eli Robins and Robert Spitzer. Dr. Spitzer had been interested in systematic diagnostic methods (Spitzer et al. 1970) for a long time. While participating in the United States-United Kingdom study of depression and schizophrenia, he had developed a systematic interview known as the Psychiatric Status Schedule. During the discussion about instruments to be used in the collaborative study, he became enthusiastic about the Feighner criteria. He, Jean Endicott, and Eli Robins worked together to modify the Feighner criteria, and their revision was called the Research Diagnostic Criteria (1975).

A number of years ago, Dr. Spitzer was given the job of leading the task force to create *DSM III*. His work with the RDC inspired him to try to give *DSM III* the same kind of rigor the RDC provided, so that diagnoses across medical centers would be more comparable than had previously been the case. Not surprisingly, he invited some of the Washington University group responsible for the Feighner criteria to help him. This author served on the substance abuse panel, which had as one of its jobs writing the section on alcohol. Other members of that group were Drs. Henry Rosett, Robert Morse, Sheldon Zimberg, and Milton Gross, who had worked with a World Health Organization (WHO) steering group on alcoholism, led by Griffith Edwards, in 1975.

Tables 3-6 show the extent to which *DSM III* evolved from RDC and Feighner criteria. On the left of the tables are the *DSM III* criteria. The center column shows similar criteria as they appeared in RDC, and, at the right, the same items in Feighner. A number of new symptoms appear in *DSM III*, representing input from a variety of persons. Symptoms that appeared in RDC and Feighner, but are not included in *DSM III* are underlined.

Criteria for Pathological Patterns of Use

One *DSM III* criterion is the need for daily use of alcohol to function adequately. This particular item has been the subject of considerable discussion because of the vagueness of "adequate function." Some researchers have been concerned that the term might be extended to include individuals who are upset if they can't have their daily drink before dinner, even though they functioned perfectly well that day without alcohol and will function well again the next day. The difficulty here is in distinguishing between a desire to preserve pleasant habits and signs of pathology.

All three systems include as one of the criteria, the inability to control one's drinking. *DSM III*, however, omits the person's own opinion as to whether he or she drinks too much, which in fact is the most common symptom found among alcoholics. Only *DSM III* includes a person's efforts to control drinking by "going on the wagon." Restricting drinking to certain times of day is found both in *DSM III* and in the Feighner criteria; Feighner also includes control by rules against drinking alone.

Binge drinking appears in all three systems, although the binge must be of somewhat longer duration in RDC than in the other two. The RDC requirement that the binge drinker consume more than one fifth a day guarantees that the individual will be intoxicated during these binges. *DSM III* also uses drinking more than a fifth a day as an indicator of pathological drinking, but the quantity

Table 3. The DSM III Criteria for the Diagnoses of Alcohol Abuse and Dependence and Their Source: I. Pattern of Pathological Alcohol Use

DSM III	RDC	Feighner
Need for daily use for adequate functioning		
Inability to cut down or stop	(3) Admits often can't stop	Group 2-(1)Not able to stop
	(1) Says he drinks too much	Group 4-(1)Thinks he drinks too much
Repeated efforts to control by 'going on wagon" or restriction to certain times of day'		Group 2-(2)Allowing himself to drink...only after 5 p.m., only on weekends,only with others
Binges (at least 2 days)	(9) Three occasions of 3 days drinking more than one fifth per day	Group 1-(4)Binges--2 days with default of obligations
Drinks more than one fifth per day		
Blackouts	(13) Frequent blackouts	Group 1-(3) Blackouts
Drinking exacerbates serious physical disorder		
Drinks nonbeverage alcohol		Group 2-(4)Nonbeverage alcohol

Key: Underlined phrases are not specifically covered in DSM III - DSM III criteria do not appear in other systems.

Table 4. The DSM III Criteria for the Diagnoses of Alcohol Abuse and Dependence and Their Source: II. Impairment in Social or Occupational Functioning

DSM III	RDC	Feighner
Violence while intoxicated	(10) Physical violence	Group 3 (4) Fighting
Absence from work	(5) Missed work, impaired job performance, unable to take care of household responsibilities	(3) Trouble at work
Loss of job	(6) Job loss	
Arrest for intoxicated behavior	(12) Picked up by police due to behavior	(1) Arrests for drinking
Traffic accidents while intoxicated	(11) Traffic difficulties due to drinking, reckless driving, accidents, speeding	(2) Traffic difficulties
Arguments or difficulties with family or friends	(2) Others complain	Group 4 (4) Others object
	(7) Frequent difficulties with family members, friends, or associates	(2) Family objects
	(8) Divorce or separation; where drinking is primary reason	(3) Lost friends

KEY: Underlined phrases are not specifically covered in DSM III - DSM III criteria do not appear in other systems.

consumed need not be associated with a binge. Thus people who drink a great deal every day and whose consumption varies little from day to day are not excluded.

Blackouts are accepted in all three systems as a sign of pathological drinking. *DSM III* includes as well drinking that exacerbates a serious physical disorder. This criterion was added to include persons whose drinking, if they were healthy, would not be pathological, but who, because of their physical state, should not drink at all. Their drinking is pathological for *them*, even though their consumption patterns are well within the social norms of the group in which they live. The difficulty with this criterion is in defining the severity of the physical illness. Clearly, many people who would like to lose weight drink, even though alcohol provides them with excess calories. Weight problems, however, generally are not classified as serious medical disorders and do not qualify individuals under this criterion.

Table 5. The DSM III Criteria for the Diagnoses of Alcohol Abuse and Dependence and Their Source: III. Tolerance to Alcohol or Withdrawal Symptoms

DSM III	RDC	Feighner
Tolerance		
Need for increased amounts to achieve desired effect or diminished effect with same amount	--	--
Withdrawal		
Morning 'shakes' and 'malaise' after cessation or reduction relieved by drinking	(14) Tremors (4) Drinking before breakfast	Group 1 (1) Tremulousness Group 2 (3) Drinking before breakfast

Criteria for Impairment of Social or Occupational Functioning

Table 6. The DSM III Criteria for the Diagnoses of Alcohol Abuse and Dependence and Their Source: IV. Medical Complications of Dependence

DSM III	RDC		Feighner	
NOT USED IN DIAGNOSIS	USED IN DIAGNOSIS		USED IN DIAGNOSIS	
			Group 1	
Hepatitis, cirrhosis	(18)	Cirrhosis	(2)	Cirrhosis
Peripheral neuropathy	(19)	Polyneuropathy	(2)	Polyneuropathy
Gastritis		--	(2)	Gastritis
Alcohol withdrawal delirium	(15)	DT's	(1)	Delirium
Alcohol hallucinosis	(16)	Hallucinations	(1)	Hallucinations
Alcohol amnestic syndrome	(20)	Korsakoff's Psychosis	(2)	Korsakoff's Psychosis
Dementia associated with alcoholism		--		--
Other Disorders				
Neurological	(17)	Withdrawal seizures	(1)	Convulsions
--		--	(2)	Myopathy
--		--	(2)	Pancreatitis

Table 4 shows the items included under social and occupational functioning, group B in alcohol abuse. Alcohol-related violence appears in all three systems, although it is more broadly defined in RDC and *DSM III* than in Feighner. Absence from work and job loss because of drinking are the only occupational impairments listed in *DSM III*; RDC and Feighner define work troubles more generally. Arrests for intoxication also are listed in all three systems, as are traffic accidents while intoxicated; again both RDC and Feighner include broader definitions of traffic difficulties. Interpersonal difficulties are mentioned in all three systems; *DSM III* globally describes these as difficulties with family and friends. RDC generally includes more detail; only Feighner includes losing friends because of drinking. Losing friends is actually a rare occurrence because people tend to choose friends with drinking patterns similar to their own.

Criteria for Tolerance and Withdrawal

Table 5 shows criteria to gauge tolerance and withdrawal, which serve only for alcohol dependence, not for abuse. Tolerance does not appear in RDC or Feighner at all; it was added to alcohol dependence in *DSM III* so that alcohol problems could be measured comparably to problems with other drugs.

Determining personal tolerance to alcohol is something of a problem. People vary enormously in the amounts they can drink even when the individuals are inexperienced drinkers. Clearly, they develop tolerance to alcohol (alcoholics regularly drink amounts no inexperienced drinker can), but it is hard to obtain evidence of this tolerance. You can ask alcoholics whether they have had to increase their intake to get a desired effect or whether they have experienced diminished effect from the same intake. But by the time alcoholics see a physician to discuss drinking, most have been tolerant at about the same level for many years. They may not remember how much less they used to drink to achieve the same effect.

DSM III restricts evidence of withdrawal to shakes and malaise relieved by drinking. These also appear in the RDC and Feighner criteria as tremors or tremulousness and drinking before breakfast.

Medical Complications as Criteria

Table 6 shows the medical complications of dependence. These are not used as diagnostic criteria in *DSM III*, although they are used in the other two systems. *DSM III* lists them as complications of dependence in the text preceding the diagnostic criteria. Their omission as diagnostic criteria is, no doubt, because of their separate enumeration under Organic Brain Syndromes. Pancreatitis and myopathy appear in the Feighner criteria, but not in *DSM III*. The authors' experience in a current study of frequency of moderate drinking in patients who were seen for an alcohol-related problem 5 to 10 years ago suggests that this omission is wise. When we checked records of medical and surgical patients with diagnoses of pancreatitis in our hospital, we found no elevated rate of problem drinking in their histories. Myopathy was too rare a diagnosis to be subjected to this kind of analysis.

How *DSM III* Diagnostic Criteria Were Constructed

The history of the *DSM III* criteria may explain some of the differences between *DSM III* and the systems from which it originated. The first draft of the *DSM III* section on alcohol abuse and dependence was written in 1975. There was little criticism of the specific criteria then, but reviewers did argue with the natural history of the disorder.

It said that alcoholics tend to have early onset and a history of antisocial behavior. Some of the reviewers treated only private patients and thought that alcoholism tended to be of much later onset and to occur frequently in people of middle-class origin. They were not impressed with its association with antisocial personality. Data from the literature were produced to convince them that their patients were somewhat atypical.

In 1976, Dr. Frank Seixas, president of the National Council on Alcoholism (NCA), reviewed the proposed criteria. He asked that the NCA definition be used instead of the one in the draft and objected to DSM III's dropping the word "alcoholism." The term "alcoholism" now appears, but only in a statement which says "Alcohol dependence has also been called alcoholism" and in the title of one of the alcohol organic mental disorders, "Dementia associated with alcoholism." Seixas particularly wanted to see psychological criteria omitted from the criteria for alcohol dependence and discussed only under alcohol abuse. Psychological dependence, disguised under the title "Pathological Use," is still part of the "A" criteria for alcohol dependence, however.

One of the reasons the *DSM III* task force resisted adopting the NCA definition was that it implied that any drinking at all after the occurrence of alcohol problems is associated with progression of the disorder. This viewpoint has been one part of NCA's battle against the findings reported in the Rand study (Armor et al. 1978). The task force felt that the NCA statement would be better if limited to *heavy* drinking.

The panel also agreed not to include prognosis as part of the criteria. In the first place, criteria for diagnosis should be applicable early in the course of an illness, before the prognosis is known. Therefore, prognosis is often not a helpful criterion. Second, there is considerable evidence that at least a few persons who have been dependent on alcohol eventually drink moderately without problems, although the number who can do so is still very much in dispute. Finally, if one included prognosis among the criteria for a diagnosis, the diagnostic criteria would have to be changed as improvement in treatment brought about changes in prognosis.

In 1976, the criterion of 1 month's duration was adopted. Initially, it was stated as 1 month's continuous or episodic use, because those working on early drafts of *DSM III* were still considering using the same criteria for licit and illicit drugs. Use of a drug for at least 1 month was intended to eliminate the person who was only an experimenter. But this criterion did not prove very useful when related to alcohol use, because almost everyone who drinks at all has been exposed to alcohol, at least episodically, for more than 1 month. Thus, the criterion has recently been changed to make the month's duration refer to "disturbance," i.e., alcohol-related *problems*, not just exposure to alcohol.

The author's research group has been devising an interview schedule to be used in the general population which make diagnoses according to *DSM III* criteria (Robins et al. 1979). While writing computer programs to make *DSM III* diagnoses, the group noticed recently that the criteria for alcohol dependence required tolerance or withdrawal and social complications, but did not mention pathological drinking. Therefore, if someone were tolerant, had withdrawal symptoms, and *said* that drinking could not be controlled, that person still would not qualify as dependent on alcohol. As a result, the panel temporarily changed the criteria by dropping social complications as a requirement. Then, however, people could be scored as positive for dependence if they had no symptoms other than tolerance. Since tolerance is probably an invariable consequence of considerable experience with alcohol, a large proportion of the population would have been diagnosable as dependent, making the diagnosis trivial. Finally, the current pattern was chosen: Tolerance alone is not enough; there must be at least some evidence of either pathological drinking or social problems as well. This saga illustrates the difficulty of writing criteria. One has to consider both the maximum case that could be missed and the minimum case that could be included; then strike some compromise between the two.

Remaining Problems

The *DSM III* criteria for alcohol dependence and abuse represent the input of a great many people trying to produce a system that reasonably reflects both research and clinical experience. But many problems with diagnosing alcohol-related disorders remain. One that comes up frequently is a consequence of the WHO idea that an alcohol disorder represents drinking in a way that is not acceptable in one's own subculture. The difficulty comes in defining exactly what the norms are for the subculture in which a particular person lives. Furthermore, what if the norms of that subculture are not compatible with good functioning? In some subcultures, such as in some fraternity houses or on some Indian reservations, the drinking norms are incompatible with optimal functioning.

Another difficulty that pertains to all drug disorders is deciding when the intake of the drug is responsible for the behavioral difficulties. Arrests, traffic accidents, suicide, or death for unexplained reasons, in someone who has ingested drugs, may or may not be the result of the drug consumption. The persons who tend to have high arrest rates, high suicide rates, and high rates of impulsive behavior also tend to use drugs and alcohol heavily. Thus, the drug or alcohol use and the event may both be caused by some pre-existing factors.

Reliability and Scalability of Alcohol Diagnoses

Although problems in diagnosing alcohol abuse and dependence remain, it would be a mistake to be pessimistic about the potential research and clinical value of the *DSM III* criteria. It is too early to have studied the efficacy of the *DSM III* criteria themselves, but the RDC and Feighner criteria from which they grew have been studied extensively.

Reliability

The author's research group performed a test-retest study (Helzer et al. 1980) of the reliability of all the Feighner diagnoses in 99 inpatients given the same interview on successive days by two psychiatrists, two lay interviewers, or one psychiatrist and one lay interviewer. Alcohol had the highest Kappa of any diagnosis tested (0.77 out of a possible 1.00). Depression had a Kappa value of 0.58; Phobia, a value of 0.53; and Mania, 0.52. These results show that psychiatrists agree with each other when they diagnose "alcoholism," as it was called in the Feighner diagnoses, and that lay interviewers can make the same diagnoses with considerable accuracy if they use the kinds of diagnostic criteria listed in *DSM III*.

Scalability

The author in another study (Robins et al. 1977) also found that the symptoms typically used to diagnose alcoholism tend to form a Gutman-type scale in which the rarer symptoms are those that require the longest period of drinking, as shown in table 7. The results come from a study of older white and black men in St. Louis. The subjects were patients of a public hospital and members of the Teamsters Union. Those who admitted to ever having been heavy drinkers (defined as drinking at least seven drinks on one occasion at least once a week for some period) were asked which alcohol symptoms they had had and over how many years they had been heavy drinkers. The more frequent the alcohol symptoms, the shorter the average history of drinking of men suffering from that symptom; the rarer the symptom, the longer the average drinking history. Men with delirium tremens, the rarest symptom, averaged 30 years of heavy drinking, while men concerned about drinking too much, which was the most common symptom, had been heavy drinkers for an average of only 17 years.

Generally, alcohol symptoms rank similarly by frequency. The most common symptoms are those of personal and family concern; the rarest are loss of employment, hospitalization, and delirium tremens. A study of alcoholics in the Veterans Administration (Gomberg 1975) shows exactly the same pattern. Symptoms of other disorders are not known to occur in such a regular pattern nor to be so well predicted by the duration of the illness. Thus, the diagnosis of alcoholism or alcohol dependence may be more reliable and valid than other common psychiatric diagnoses.

Table 7. Symptoms and Duration of Heavy Drinking in Heavy Drinkers, Aged 45-64

Symptom	Percentage with this Symptom	Median Years of Heavy Drinking with This Symptom
1. DT's	7	30
2. Hospitalization for drinking problem	15	27
3. Lost job because of drinking	16	26
4. Drinking led to arrest	19	26
5. Trouble on job from drinking	21	25
6. Benders (more than 2 days without sobering up)	25	22
7. Trouble with wife over drink	28	22
8. Family objected on his drinking	38	21
9. Felt quilty about his drinking	41	20
10. Felt he drank too much	53	17

Finally, it is important to note that the *DSM III* diagnostic system allows multiple diagnoses. The author's research group at Washington University is currently applying the *DSM III* diagnosis of alcoholism to their data bank of studies to see what additional diagnoses persons with a diagnosis of alcohol dependence would qualify for. Our data bank now includes almost 3,000 protocols, listing psychiatric symptoms in a variety of subjects including emergency room cases, inpatients, clinic patients, and relatives of patients. As shown in table 8, the emergency room cases produced the highest proportion of alcoholism diagnoses, with inpatients and clinic patients following, in that order. Relatives of patients had the lowest rate, 10 percent. This rate is probably somewhat above that of the general population, as one would expect, because many are relatives of alcoholic patients.

Table 9 lists other disorders diagnosed in alcoholics and compares their diagnostic patterns with those of other members of the same study. Among patients who were not alcoholics, there had to be at least one diagnosis, just to explain their presence in treatment. Consequently, emergency room and inpatients who were not alcoholics tended to have somewhat higher rates for other diagnoses than did the alcoholics. What is interesting is that despite this "other" diagnosis, they were less likely to have antisocial personality than were the alcoholics. These results support the *DSM III* text, which notes the association between alcoholism and antisocial personality.

Table 8. Diagnoses From a Data Bank (Percent of Patients)

	Type of Study			
Disorders	Emergency Room Patients	Inpatients	Clinic Patients	Relatives of Patients
Total N	(314)	(221)	(500)	(1357)
Alcoholism	33%	28%	13%	10%
Depression	37	75	50	7
Panic	10	23	21	5
Somatization	5	18	8	2
Antisocial personality	15	11	6	3

It is also of interest that both inpatients and clinic patients who are alcoholics had more Panic Disorder (what used to be called Anxiety Neurosis) than did other patients. And in nonpatients, that is, in the relatives of patients, alcoholism was associated with an increased rate of *every* other disorder, suggesting that the presence of *any* psychiatric disorder may make it more likely that one will also have at least one other problem.

Alcoholics as inpatients or clinic patients tend to be depressed. Alcoholics generally don't seek care in psychiatric facilities unless they have concurrent depression. Depression is less frequent in cases brought to the emergency room because of public inebriation.

Table 9. Data Bank Studies: What Other Disorders Do Alcoholics Have? (Percent of Patients)

Type of Patients	No. of Patients	Depression	Panic	Somatization	Antisocial Personality
Emergency Room					
Alcoholics	105	31	8	3	27
Others	209	40	12	7	10
Difference		−9	−4	−4	+17
Inpatients					
Alcoholics	61	69	32	13	20
Others	160	77	19	19	8
Difference		−8	+13	−6	+13
Clinic Patients					
Alcholics	65	54	32	8	17
Others	435	49	20	8	4
Difference		+5	+12	0	+13
Relatives of Patients					
Alcoholics	135	17	7	6	11
Others	1,222	6	5	1	3
Difference		+11	+2	+5	+8

In conclusion, the story of the development of the DSM-III diagnoses relating to alcohol intake reveals the logical complexities of describing the mixture of physical, social, and psychological correlates of using alcohol that constitute our diagnostic criteria. Some of these correlates are clearly effects of alcohol intake, while others, particularly the antisocial acts seen in heavy drinkers, may often be what DSM-III calls "associated features"—as often indicators of personality types predisposed to heavy drinking as consequences of the drinking itself. Some of these correlates, such as auto accidents, can occur in response to a single ingestion of large amounts, while others, like DTs and cirrhosis, require years of exposure.

It is remarkable, given these logical difficulties, the assembling of symptoms from grossly different conceptual realms, and the reported unreliability of alcoholics as historians, that the diagnosis of alcoholism by symptom self-report is repeatedly found to be one of the most valid and reliable of the psychiatric diagnoses. There seems little doubt that crude as our methods remain, despite the efforts of the DSM-III task force, we are tapping a sturdy entity with our counting of social, medical, and psychological alcohol problems.

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DISCUSSION OF PAPERS BY CADORET, COSTELLO, AND ROBINS

Bernard Glueck

The three papers in this session present three quite different approaches to the problem of understanding the relationship between alcohol abuse and other psychopathological conditions. The diverse approaches indicate the difficulties alcoholism researchers encounter.

In the first paper, Dr. Cadoret examines the association between various types of depressive symptoms and two types of alcoholics, primary and sociopathic. He then examines certain variables, such as suicide and years of drinking in the different groups, in an attempt to create some kind of typology that would be useful diagnostically, and perhaps prognostically, in the treatment of future patients. This approach has been used frequently in many studies that sought to define significant subtypes of alcoholics and to ascertain the association between alcoholism and other psychopathology. Most of these studies, including this one, suffer from a problem of relatively small sample size, thus admitting the possibility of serious skewing of the findings. Adequate replication with new populations is also difficult to perform, for a variety of reasons. However, these efforts to utilize significant clinical data to further our understanding of the problems of the alcoholic patient have provided us with significant amounts of information that have formed much of the basis for the construction of diagnostic classifications that will be utilized in the *DSM III* of the American Psychiatric Association.

Dr. Costello discussed the problems involved in diagnosis and in the development of classification schemes. He issued a number of caveats about using various types of inventories, questionnaires, and checklists, and was especially concerned with redundancy within the instruments, or across several testing instruments. He also warned against using a computer and complicated statistical procedures to try to define an organizational principle or classification rule. His basic argument was that the clinician-researcher, using scores from standardized tests and complicated statistical procedures, must begin with some theory-based typology before making statistical analyses of the data. Dr. Costello then discussed data collected from scores on Cattell's 16 Personality Factor test, given to 120 subjects. Investigators using multivariate statistical approaches to create significant typologies, either to better understand the alcoholic patient or to look at personality or psychopathology in general, will find the paper helpful.

The third paper, by Dr. Robins, provides us with a detailed description of the struggles involved in attempting to formulate a useful classification scheme for individuals with alcohol problems. Lee Robins was a member of the task force assigned this particular problem from the beginning of the development of *DSM III.* The diagnostic categories that resulted may not be entirely satisfactory for all cases, and will not be particularly pleasing to some clinicians with different theoretical orientations about the causes of alcoholism. Nevertheless, the procedures developed by Dr. Spitzer and his colleagues and adopted by the various task force subgroups for *DSM III,* merit careful consideration. As Dr. Robins points out, the task forces attempted to utilize the information available in the different diagnostic areas to develop a series of classifications that would cover the clinical case material adequately without becoming too atomistic, and therefore unworkable. They have attempted to avoid classification schemes based on psychodynamic or physiologic theories, and have, instead, chosen to follow clinical observations, in so far as it was possible. The result is a series of diagnostic statements that describe certain behavioral patterns and historical patterns that are prerequisite to the assignment of a particular diagnosis. From my standpoint as a clinician-researcher, I feel that the present schema, as presented in *DSM III,* will help sharpen our diagnostic concepts and will go a long way toward relieving much of the confusion that presently exists about our classification system. Each person making a diagnosis will be required to document this using a set of observations and definitions that can be agreed on by clinicians, and that can be fairly readily taught. Following the criteria should provide greater uniformity in the classification of patients, and therefore will improve our ability to compare studies by different clinicians in different treatment settings.

SESSION III: ALCOHOLIC PEDIGREE, SEX DIFFERENCES, AND THE PROBLEM OF RISK

FAMILY HISTORIES OF MALE AND FEMALE ALCOHOLICS

Donald W. Goodwin

Alcoholism: A Family Disease

Historical Background

The idea that alcoholism runs in families dates back to antiquity. Aristotle declared that drunken women "bring forth children like themselves." Plutarch said "one drunkard begets another" (Burton 1906). During the "gin epidemic" in 18th-century England, the notion that alcoholism was not only familial but hereditary was strong, with many tracts denouncing consumption of spirits on the grounds that it produced alcoholism in the offspring (Warner and Rosette 1975). In the early 19th century, Benjamin Rush, holding similar views, warned against prescribing alcohol to pregnant women (Rush 1787), and throughout the 19th century numerous references appeared in medical and religious works referring to the transmission of alcoholism from generation to generation.

Fournier (1877) believed, as did many of his generation, that alcoholism promoted not only alcoholism in subsequent generations, but also other forms of "depravity," most conspicuously mental retardation. He wrote, "It is common to witness the son of a drunkard becoming addicted to excess in drinking at an early age, but the principle of transmission does not confine manifestations to a reiteration of the same form of derangement but other phenomena of disordered nerve elements are legitimately traced in children through many generations back to a drunken progenitor." Although it was agreed that alcoholism ran in families, not everyone agreed that alcoholism was associated with other illnesses. As will be noted later, this controversy still persists.

Systematic Studies

Late in the 19th century, investigators for the first time began systematic studies of the families of alcoholics. Previously, the evidence had been entirely anecdotal. One of the first systematic studies was conducted by Long (1879), who questioned 200 Michigan doctors about the offspring of alcoholics. They attributed about 21 percent of "inherited disease" to alcohol, but did not identify the diseases. Shuttleworth and Beach (1900) found alcoholic parentage in 19 percent of the idiots at a paupers home and in 13 percent of the residents at a charitable institution. MacNicholl (1905) surveyed the schoolchildren of New York City in one of the largest studies of alcohol as a cause of mental retardation ever attempted. He found that of 6,624 children of drinking parents 53 percent were retarded, whereas among 13,000 children of abstainers, only 10 percent were retarded.

In 1909, Crothers reported that of 4,400 inebriates he treated during 35 years in practice, 70 percent had ancestors who drank moderately or excessively. In the first two decades of the century, several other investigators reported similar findings, with only one exception. Elderton and Pearson (1910) reported that children of alcoholics were as normal as children of nonalcoholics. As Warner and Rosette (1975) commented in their review, that study led to heated controversy, with opponents criticizing the investigators for using moderate drinkers rather than abstainers as a control group and for failing to determine whether the parents' drinking began before or after the birth of the children studied. Even John Maynard Keynes criticized the study on statistical grounds.

With this one exception, every family study of alcoholism, regardless of country of origin, has shown a much higher rate of alcoholism among the relatives of alcoholics than generally occurs in the general population.

For instance, Boss (1929), examining the siblings and parents of 909 male and 166 female alcoholics, found that alcoholism occurred in 53 percent of the fathers, 6 percent of the mothers, 30 percent of the brothers, and 3 percent of the sisters. Pohlisch (1933) compared the siblings and parents of chronic alcoholics with the siblings and parents of opiate addicts with respect to alcoholism and morphinism. Alcoholism was found in 22 percent of the brothers of alcoholics and in 6 percent of the brothers of opiate addicts. Alcoholism occurred in 47 percent of the fathers of alcoholics and in 6 percent of the fathers of opiate addicts. Conversely, among the parents and siblings of opiate addicts, opiate addiction occurred more frequently than did alcoholism. Studying a large sample of alcoholics and their families, Brugger (1934) found that about 25 percent of the fathers were alcoholic. Other authors reporting similar figures are Amark (1953), Gregory (1960), and Winokur and Clayton (1968). Viewing the situation from another aspect, Dahlberg and Stenberg (1934) reported that 25 percent of hospitalized alcoholics came from families in which one of the parents abused alcohol.

The lifelong expectance rate for alcoholism among males appears to range from about 3 to 5 percent; the rate for females is from 0.1 to 1 percent (Goodwin 1971). A study by Winokur et al. (1970) showed a particularly high prevalence of alcoholism among the full siblings of alcoholics. Among the full siblings of male alcoholics, there was a lifetime expectancy of excessive drinking in 46 percent of the brothers and in 5 percent of the sisters; the lifetime expectancy of alcoholism among the full siblings of female alcoholics was 50 percent in the brothers and 8 percent in the sisters. These expectancy rates are higher than those reported in most other studies, possibly because the investigators studied family members rather than relying solely on information from alcoholic probands. A study by Rimmer and Chambers (1969) showed that "family studies" in which family members are interviewed reveal higher rates of alcoholism than do "family history studies," in which only alcoholic probands are interviewed.

In all, according to a recent review by Cotton (1979), some 140 estimates of the familial incidence of alcoholism are now in the literature. Of these, Cotton eliminated about 50 because they were in journals published in languages other than English. Of the remainder, 39 sufficiently describe the source of subjects, sample size, sex of subjects, geographic scope of study, source of information, definition of alcoholism, and relationship of family member to alcoholic to be even roughly useful for comparative purposes. Only eight studies had controls, such as data on the incidence of alcoholism in the families of both alcoholics and nonalcoholics. Nonalcoholics include populations of nonpsychiatric patients from surgical and medical wards, patients with a variety of psychiatric diagnoses, and persons who were neither patients nor problem drinkers.

Two-thirds of the studies found that at least 25 percent of alcoholics had fathers who were alcoholics. Fathers and brothers of alcoholics were more likely than mothers and sisters to be alcoholics. According to half of the estimates, maternal alcoholism occurred in fewer than 5 percent of the alcoholics' families. In the remaining studies, reported incidence ranged from 6 percent to 20 percent in the alcoholics' families. Many studies reporting data on fathers failed to report comparable data on mothers.

Most of the studies reviewed by Cotton reported only the incidence of alcoholism in subjects' parents; 18, however, also reported high rates of alcoholism in siblings, and 8 reported high rates among other relatives. Rates of sibling alcoholism were reported as the number of alcoholics in the total number of siblings, or as the number of patients having one or more siblings who were alcoholics. In either case, rates of sibling alcoholism were consistently higher in samples of alcoholics than in all types of nonalcoholics studied. Naturally, rates of parents are not comparable with those of siblings; the parents have passed through a much longer period of risk. As many as 62 percent of one sample of alcoholics had one or more relatives in the preceding two generations who had "problems with alcohol." Three-quarters of another sample of hospitalized alcoholics reported alcoholism in first-degree relatives. In most studies, the incidence of alcoholism in first-degree relatives was higher than that of more distant relatives of alcoholics.

In nine studies comparing rates of alcoholism in families of women versus families of men alcoholics, seven show higher rates in the families of women than in those of men. In one study, for example, approximately one-half of the women and one-third of the men alcoholics came from families in which at least one parent was an alcoholic; only 9 percent of the siblings of men alcoholics, compared with 24 percent of the siblings of women alcoholics, were alcoholics. Cotton interpreted the finding that women alcoholics are more likely than men alcoholics to come from families in which pathological drinking has occurred as indicating that women are more vulnerable than men to the impact of familial alcoholism. Another explanation is that existing social barriers to heavy drinking by women require a heavier "genetic load" for alcoholism to emerge in women members of the family.

All comparisons of samples of alcoholics and nonalcoholics reveal lower frequencies of parental alcoholism in the families of nonalcoholics. Even when the nonalcoholics were psychiatric patients, the rates of familial alcoholism were low. Winokur et al. (1970), for example, were able to find only a 9.5 percent incidence of parental and a 1.1 percent incidence of maternal alcoholism in the parents of 366 patients with affective disorders. Thus, as Cotton points out, a high rate of parental alcoholism is not merely specific to disturbed populations, but a characteristic of populations of alcoholics. Parental alcoholism usually ranges from 1 to 2 percent in the nonpsychiatric samples reviewed, and maternal alcoholism never exceeds 1 percent of the mothers of any of the samples of nonalcoholics.

These rates are similar to the rates of alcoholism expected in general populations, based on five studies of nonalcoholics in the general population (Goodwin 1971).

Aware that "familial" does not necessarily mean "hereditary," several of the authors cited attempted to analyze their data to control for environmental factors. Dahlberg and Stenberg (1934) established that one of the parents of their alcoholics was, in 25 percent of the cases, alcoholic, and that both parents were abstainers in 12 percent of the cases. The severity of alcoholism was the same if the parents were alcoholics or abstainers. The authors interpreted this finding as indicating a hereditary influence in alcoholism. Amark (1953) reported that "periodic" and "compulsive" alcoholics more frequently had alcoholic children than did alcoholics whose illnesses presumably were less severe. Home environments were found to be equally "good" or "bad" in both groups, again suggesting that alcoholism had a hereditary component. Utilizing a pedigree approach to an investigation of a single large family, Kroon (1924) concluded that alcoholism was influenced by a sex-linked hereditary trait—a subject that will be discussed later in the section about genetics.

Alcoholism also has been studied with regard to its possible association with other psychiatric illnesses. According to several studies (Brugger 1934; Amark 1953; Bleuler 1932; Winokur et al. 1970; Guze et al. 1967), excess depression, criminality, sociopathy, and "abnormal personality" seem to appear in the families of alcoholics. Typically, depression occurs most often in female relatives and alcoholism or sociopathy in males. Relatives of alcoholics apparently were no more often schizophrenic, mentally defective, manic, or epileptic than were relatives of nonalcoholics.

Proposed Explanations for Genetic Transmission

Pre-Darwinian Explanations

From Biblical times until the theories of Darwin were accepted in the late 19th century, there were two explanations for offspring of alcoholics either to be alcoholic or to suffer from some other "degenerative" disease or "depravity." One was theological, reflecting the Biblical belief that "the sins of the fathers are visited upon the sons," and the other was naturalistic.

The naturalistic view, held by Aristotle, Plato, and other writers of antiquity, as well as by many subsequent generations of physicians including Benjamin Rush and other 19th-century writers, was based on the Lamarckian theory of the inheritance of acquired characteristics. The children of alcoholics became alcoholic or suffered other disorders because (a) one or both of their parents drank alcohol at time of conception or (b) the mother drank alcohol during pregnancy. Drinking during pregnancy has been discouraged by many societies, including Carthage and Sparta, both of which had laws prohibiting the use of alcohol by newly married couples. The Bible also warned against imbibing during pregnancy; an angel appeared to Samson's mother and informed her that she would become pregnant and should not drink wine during the pregnancy (Judges 13:4, cited in Warner and Rosette 1975).

With the advent of modern medicine in the 17th and 18th centuries, physicians frequently expressed their belief in the deleterious effects of alcohol on the germ cell or fetus. Morel (Warner and Rosette 1975) stated that parental drunkenness produced depravity, excessive use of alcohol, and degradation in the first generation of offspring, with progressively more severe symptoms in their children, until the fourth generation produced sterility, heralding extinction of the line. Bezzola (1901) proposed that alcohol caused damage to the germ cell, resulting in idiot children. Studying birth records in Switzerland, he found an increase in the birth of idiots 9 months after wine festivals, with a corresponding drop in normal births.

Rarely, if ever, was a nonbiological explanation given for the alcoholism "taint" running through families. Even theologians tended to ascribe the transmission of alcoholism from generation to generation to a toxic effect of alcohol on the germ cell or fetus. It is difficult to find an environmental explanation for alcoholism until the second or third decade of the 20th century, when emphasis shifted to social factors in mental illness and Lamarckian genetics virtually disappeared (except in Russia).

Environmental Explanations

Biological explanations for mental illnesses waned, coincident with the rise of social work, sociology, child-rearing systems, and psychological theorists such as Freud and the behaviorists. By 1940, these influences had become so strong that such distinguished students of alcoholism as E.M. Jellinek, having reviewed the evidence for a genetic factor in alcoholism, categorically stated that there is none (Jellinek and Jolliffe 1940). With rare exceptions, interest in identifying biological factors in alcoholism was in eclipse from roughly 1930 through the 1950s.

Environmental explanations for alcoholism were numerous and varied. (a) The parents are "bad" parents. They frustrate the child, making him feel anxious in later life. He drinks to feel less anxious. (b) The family "teaches" the child to drink. The boy sees his father drink and follows his example. He learns from observation that certain problems can be solved by drinking: fatigue, depression, shyness. (c) The values of the family are transmitted to the child, and these values promote drinking. For example, young men who cannot cry because of the "machismo" they learned from their fathers may find that alcohol provides consolation for occasions when crying would be consoling. The evidence supporting these theories ranges from a little to none at all (Goodwin 1976).

Today, it is fashionable to blame alcoholism on multiple factors—biological, sociological, psychological. In some ways, alcoholism is clearly related to various causes. Genes give us enzymes to metabolize alcohol; society gives us alcohol to metabolize; and our psyches respond in specific ways to these combined factors. Nevertheless, beyond this obvious level, the evidence for multiple causes of alcoholism is no better or worse than the evidence for a single cause. The cause of alcoholism, in truth, is unknown. But it *does* run in families and this is a starting point.

Genetic Explanations

"Familial," of course, is not synonymous with "hereditary." Speaking French may also be familial, but presumably not because of genes. Nevertheless, in studying familial disorders, it is important to determine whether the illness is influenced by heredity. Unless the illness follows a precise Mendelian mode of inheritance, such as Huntington's chorea does, separating "nature" from "nurture" is difficult. The temptation, however, to attempt to disentangle the two is apparently strong: nature-nurture studies are still popular, despite widespread skepticism about their feasibility.

The main problem in assessing the relative importance of heredity and environment is that both are usually provided by an individual's progenitors, at least early in life. Through the years, a number of strategies have been developed to circumvent this problem with regard to alcoholism. In general, these can be grouped into three types: (a) twin studies, (b) adoption and half-sibling studies, and (c) genetic marker studies. The first two approaches will be examined here.

Twin Studies

One method for evaluating whether genetic factors may predispose individuals to a particular disease is to compare identical with fraternal twins, where at least one member of each pair has the illness. Originally proposed by Galton, this approach assumes that monozygotic and dizygotic twins differ only with respect to genetic makeup, and that environment is as similar for members of a monozygotic pair as for a dizygotic pair. Given these assumptions, the prediction is that genetic disorders will be concordant more often among identical twins than among fraternal twins.

The twin approach has been applied to alcoholism in two large-scale studies—one Swedish, the other Finnish. In the former, Kaij (1960) located 174 male twin pairs where at least one partner was registered at a temperance board because of a conviction for drunkenness or other indicator of alcohol abuse. Kaij personally interviewed 90 percent of the subjects and established zygosity by anthropometric measurements and blood types. The concordance rate for alcohol abuse in the monozygotic group was 54 percent; in the dizygotic group it was 28 percent, a statistically significant difference. Moreover, by dividing alcohol abusers into subgroups based on severity, the largest contrast occurred among individuals with the most extensive use of alcohol.

Kaij also found that social and intellectual "deterioration" was more correlated with zygosity than with extent of drinking; a "deteriorated" heavy-drinking monozygotic twin was more likely to have a light-drinking partner showing signs of deterioration than were dizygotic twins where one partner had deteriorated. He interpreted this finding as indicating that "alcoholic deterioration" occurred more or less independently of alcohol consumption and may be a genetically determined contributor to the illness rather than a consequence.

In the Finnish study, Partanen et al. (1966) found more equivocal evidence of a genetic predisposition to alcoholism. They studied 902 male twins, 28 to 37 years of age, a substantial proportion of all such twins born in Finland between 1920 and 1929. Zygosity was determined based on anthropometric measures and serological analyses. The authors also studied a sample of brothers of the same age as the twins. Little difference was found in within-pair variation between dizygotic twins and the nontwin brothers. Subjects were personally interviewed and evaluated with personality and intelligence tests.

In contrast to Kaij, Partanen et al. (1966*b*) found no difference between monozygotic and dizygotic twins with regard to consequences of drinking (perhaps the most widely accepted basis today for diagnosing alcoholism). More or less normal patterns of drinking, however, did appear to reflect genetic factors. Frequency and amount of drinking were significantly more concordant among monozygotic twins than among dizygotic twins. Abstinence also was more concordant among identical twins. However, the authors found no signs of heritability for the presence of "additive" symptoms, arrests for drunkenness, or various social complications of drinking.

A third twin study was conducted in the United States, utilizing questionnaire data. Leohlin (1972) studied 850 pairs of like-sex twins chosen from a group of some 600,000 high school juniors who took the National Merit Scholarship Questionnaire Test. Included in the questionnaire were 13 items related to attitudes toward alcohol and drinking practices. Also included were items permitting a rough approximation of zygosity. Leohlin found that putative monozygotic twins were more concordant for "heavy drinking" than were putative dizygotic twins. Drinking customs and attitudes toward drinking appeared to be uninfluenced by zygosity. Leohlin conceded that his data were "somewhat fragile" but suggestive.

Jonsson and Nilsson (1968) reported findings based on questionnaire data obtained from 7,500 twin pairs in Sweden. Zygosity diagnoses were known for about 1,500 pairs. Monozygotic twins were significantly more concordant with regard to quantity of alcohol consumed than were dizygotic twins. Social-environmental factors, on the other hand, seemed to explain much of the variation in consequences from drinking, a result corresponding closely to that reported in the Partanen et al. study (1966).

Vesell et al. (1971) studied the elimination rates of alcohol in 14 pairs of twins. The subjects were given 1 ml/kg of 95 percent ethanol solution orally; the ethanol elimination rate was measured by taking blood samples during a 4-hour period. The researchers found that the heritability value for the ethanol elimination rate was 0.98. In short, the rate was almost totally controlled by genetic factors.

Forsander and Eriksson (1974) compared six monozygotic and eight dizygotic male twin pairs in Finland. A heritability value of 80 percent was found for ethanol elimination rates, and a value of 60 to 80 percent for acetaldehyde in venous blood. Based on these two studies, it appears that the alcohol elimination rate is under a high degree of genetic control, although further studies with larger samples must confirm this.

Like all approaches to the nature-nurture problem, twin studies have a number of weaknesses. For example, the assumption that identical and fraternal twins have equally similar environments is open to question. In Partanen's study, identical twins differed from fraternal twins in that the identical twins lived longer together, were more concordant with respect to marital status, and were more equal in "social, intellectual, and physical dominance relationships." Even in rare instances where monozygotic twins are reared apart, zygosity may influence environmental effects, that is, personal appearance influences people's behavior toward an individual—thus, people who look alike may be treated alike. In this and other ways, the interaction between physical characteristics and the environment may tend to reduce intrapair differences in identical twins and increase differences in fraternal twins.

Furthermore, twins represent a genetically selected population (Partanen et al. 1966). They have higher infant mortality, lower birth weight, slightly lower intelligence, and their mothers are older.

Adoption Studies

Another approach to separating "nature" from "nurture" is to study individuals separated from their biological relatives soon after birth and raised by nonrelative foster parents. Beginning in 1970, the author and his colleagues started a series of adoption studies in Denmark supported by the National Institute on Alcohol Abuse and Alcoholism. The researchers designed to investigate the possibility that alcoholism in part has genetic roots (Goodwin et al. 1973; Goodwin et al. 1974). The studies have gone through three phases, the most recent one completed in 1977.

Phase One. Because men are more likely to develop drinking problems than are women, the first phase of the research involved studying a sample of Danish males who had a biological parent with a hospital diagnosis of alcoholism and who had been adopted by nonrelatives in the first few weeks of life. The control group, consisting of age-matched men without, as far as was known, alcoholism in their biological parents, was selected from a large pool of adoptees. A psychiatrist interviewed the sample of 133 men, average age 30; 55 had a biological parent who was alcoholic. These 55 were matched with 78 controls whose parents had no known alcoholism. Some may have had alcoholic parents, but there was no record of this fact in the central registries maintained in Denmark. The interviewer did not know whether the interviewees were sons of alcoholics or sons of presumed nonalcoholics, and the study was "blind" from its inception until the data were analyzed. Experimenter bias, therefore, could not have been a factor in the study.

The results of the study can be summarized as follows.

1. Ten of the 55 probands (sons of alcoholics) were alcoholic, according to both specific criteria and a history of treatment for alcoholism. Of the 78 controls, 4 met the criteria for alcoholism, but none had received treatment. The difference was significant at the 0.02 level.

2. The probands were no more likely to be heavy drinkers or drinkers with occasional problems from drinking than were the controls. About 40 percent of each group were heavy drinkers, defined as daily drinkers who drank six or more drinks at least several times a month. Having a biological parent who was alcoholic increased the likelihood of the son's being alcoholic, but did not increase the chance of his being classified as a heavy drinker.

3. The interviewer, a trained psychiatrist, obtained a complete psychiatric history and performed a mental status examination. The probands were no more likely to receive a diagnosis of depression, sociopathy, drug abuse, or other diagnosable psychiatric condition than were the controls. Both groups had sizable numbers of individuals diagnosed as having various personality disturbances, but these vaguely described traits were as common in the control group as in the probands.

From these data, it was concluded that sons of alcoholics were about four times more likely to be alcoholic than were sons of nonalcoholics, despite having no exposure to the alcoholic biological parent after the first few weeks of life. Moreover, they were likely to be alcoholic at a relatively early age (in their 20s) and have a form of alcoholism serious enough to warrant treatment. Having a biological parent who was alcoholic apparently did not increase their risk of developing psychiatric disorders other than alcoholism or of being predisposed to heavy drinking in the absence of alcoholism. The familial predisposition to alcoholism in this group was *specific* for alcoholism and *not on a continuum* with heavy drinking.

Phase Two. Some of the probands had brothers who had been raised by their alcoholic biological parents. (Most of the alcoholic parents, by the way, were fathers.) The sons of alcoholics raised by their alcoholic biological parents also had a high rate of alcoholism, when compared with controls consisting of nonadopted men raised by nonalcoholic parents. The rate of alcoholism for sons of alcoholic parents raised by these parents, however, was no greater than was the rate observed in their brothers raised by nonalcoholic foster parents (about 18 percent in both groups).

The conclusion from the first two phases was that alcoholism was transmitted in families and that the increased susceptibility to alcoholism in men occurred about equally in men raised by their alcoholic biological parents and in men raised by nonalcoholic foster parents. In other words, if indeed there were a genetic predisposition to alcoholism, exposure to the alcoholic parent did not appear to augment this increased susceptibility.

Phase Three. The final phase of the study involved studying the daughters of alcoholics, both those raised by foster parents and those raised by their alcoholic biological parents. The sample consisted of 49 proband women (adopted-out daughters of alcoholics) and 48 controls (adopted-out daughters of presumed nonalcoholics). As was the case of the former studies, the interviews were conducted blindly, with no chance of biased results. The subjects were between the ages of 30 and 41, with a mean age of 35. The major findings were as follows.

1. One of the probands was clearly alcoholic and another was a serious problem drinker who failed to meet completely the criteria for alcoholism. Two of the controls were alcoholic. The three women diagnosed as being alcoholic had all received treatment for their alcoholism. Hence, 4 percent of the women in both groups were either alcoholic or serious problem drinkers. The sample was too small to draw definite conclusions from this finding, but there is an estimated prevalence of alcoholism among Danish women of about 0.1 to 1.0 percent, so the data suggest that there may indeed be an increased prevalence of alcoholism in the two groups. Nothing is known about the parents of the control women, other than that none of the controls had a biological parent with a hospital diagnosis of alcoholism; thus, the two alcoholic controls may have had parents with alcohol problems. The parents could not be located and there was no way to determine whether or not they were alcoholics. However, it was interesting that both of the alcoholic controls had foster parents who were described as alcoholic, suggesting environmental exposure to alcoholism may contribute to alcoholism in women but not to alcoholism in men.

2. More than 90 percent of the women in both groups were abstainers or very light drinkers. This finding contrasted with the Danish male adoptees; about 40 percent of the latter were heavy drinkers.

3. Family history studies have suggested that alcoholics often have male relatives who are alcoholic or sociopathic and female relatives who are depressed (Winokur et al. 1970). In this study, complete psychiatric histories were obtained and mental status examinations performed. Among the adopted women, there was a low rate of depression in both groups, with no more depression in the daughters of the alcoholics than in the controls. Among daughters of alcoholics raised by their alcoholic parents, depression was significantly more present than in controls. There was no evidence of increased susceptibility to other psychiatric disorders in the daughters of alcoholics, whether raised by foster parents or by their own alcoholic biological parents.

It appears, therefore, that alcoholism in women may have a partial genetic basis, but sample size in the present study precluded any definitive conclusion. The great majority of the women were very mild drinkers, so it is possible that social factors discouraging heavy drinking may suppress a genetic tendency, if one exists.

There was no evidence of a genetic predisposition to depression in the daughters of alcoholics. At any rate, if such a predisposition exists, apparently environmental factors are required to make the depression clinically manifest. It is not possible to determine whether the increased rate of depression of daughters raised by their alcoholic parents was due to environmental factors precipitating a genetic predisposition, or due entirely to environmental factors.

It should be noted that some evidence indicates that women develop alcoholism at a later age than men do; possibly the 35-year-old women had not all entered the age of risk for alcoholism. Followup studies are needed to explore this possibility.

Four similar studies have been conducted. Roe (1944) obtained information about 49 foster children in the 20 to 40 year age group, 22 of nonalcoholic parentage and 27 with a biological parent described as a "heavy drinker." Among children with heavy-drinking parents, 70 percent were users of alcohol, compared with 64 percent in the control parentage group. In adolescence, two children of "alcohol-parentage" got into trouble because of drinking too much, as compared with one in the "normal-parentage" group. The authors found that adopted children of heavy drinkers had more adjustment problems in adolescence and adulthood than did adopted children of nonalcoholics, but the differences were not significant and neither group had adult drinking problems. The researchers concluded that there was no evidence of hereditary influences on drinking.

This conclusion, however, can be questioned on several grounds. First, the sample was small. There were only 21 men of "alcoholic" parentage and 11 of "normal" parentage. Women, particularly at the time of the study, were at very low risk ages for alcoholism; discovering they had no problem with alcohol was not unexpected. Second, although the biological parents of the proband group were described as "heavy drinkers," it is unclear how many would justify a diagnosis of alcoholism. Most had a history of antisocial behavior, and apparently none had been treated for drinking problems. All of the biological parents of the proband group in the Danish study received a hospital diagnosis of alcoholism, at a time and place where that diagnosis was rarely assigned.

Schuckit et al. (1972) also studied a group of individuals reared apart from their biological parents where either a biological parent or a "surrogate" parent had a drinking problem. The subjects were significantly more likely to have a drinking problem if their biological parent was considered alcoholic than if their surrogate parent was alcoholic. Studying 32 alcoholics and 132 nonalcoholics, most of whom came from broken homes, showed that 62 percent of the alcoholics had an alcoholic biological parent, compared with 20 percent of the nonalcoholics. This association occurred regardless of personal contact with the alcoholic biological parent. Simply living with an alcoholic parent appeared to have no relationship to the development of alcoholism.

Bohman (1978) studied 2,000 adoptees born in Sweden between 1930 and 1949. Official registers were inspected for notations about alcohol abuse and criminal offenses in the adoptees and their biological and adoptive parents. A significant correlation appeared between registrations for alcohol abuse among biological parents and their sons released for adoption, but registered criminality in the biological parents did not predict criminality or alcoholism in the adopted sons. The higher the number of registrations for alcoholism in the biological parents, the greater the incidence of registration for alcohol abuse in the adopted children. These results support a genetic hypothesis for the development of alcoholism and closely parallel those found in the Goodwin et al. (1973) study of adopted sons of alcoholics.

Cadoret and Gath (1978) studied 84 adult adoptees (18 years old or older) separated at birth, with no further contact with their biological relatives. Alcoholism occurred more frequently in the adoptees whose biological background included an individual with alcoholism than it did in adoptees without this biological background. Alcoholism did not correlate with any other biological parental diagnosis. Childhood "conduct disorder" was significantly higher in those adoptees who later received a diagnosis of alcoholism or problem drinking.

Both of the above adoption studies produced results similar to those of the Danish adoption studies (Goodwin et al. 1973). In other words, alcoholism in the biological parents predicted alcoholism in their male offspring raised by unrelated adoptive parents, but did not predict other psychiatric illness such as criminality. In both the Danish studies (Goodwin et al. 1975) and the Cadoret and Gath study (1977), alcoholics had an increased incidence of childhood "conduct disorder," but no higher incidence of other psychopathology.

Two studies have been reported bearing on possible genetic modes of transmission. Kaij and Dock (1975) tested the hypothesis of a sex-linked factor influencing the occurrence of alcoholism by comparing alcohol abuse rates in 136 sons of the sons versus 134 sons of the daughters of 75 alcoholics. No substantial difference between the groups of grandsons was found in frequency of alcoholism, suggesting a sex-linked factor was not involved. The total sample was also used to calculate the risk of registration for alcohol abuse among the grandsons; rate of registration by the grandsons' fifth decade of life was 43 percent, approximately three times that of the general male population. This result is incompatible with an assumption of a recessive gene being involved in alcoholism, although it does fit with the assumption of a dominant gene.

Investigating the possibility that children of alcoholics metabolize alcohol differently than do children of nonalcoholics, Utne et al. (1977) compared the disappearance rate of blood alcohol in two groups of adoptees, 10 of whom had a biological parent who was alcoholic and 10 of whom came from nonalcoholic parentage. No significant difference in the elimination rate of ethanol was found.

There has been speculation that a genetic factor influencing the development of alcoholism might involve atypical liver alcohol dehydrogenase (ADH). Recent data (Stamatoyannopoulas et al. 1975) indicate a high frequency of ADH polymorphism among Japanese persons. Analysis of 40 autopsied liver specimens showed that 34 had atypical ADH phenotype. There appears to be a relatively low rate of alcoholism in Orientals, so the fact that possibly 85 percent of the Japanese population carries an atypical liver ADH suggests that alcohol sensitivity may result from increased acetaldehyde formation in individuals carrying an atypical ADH gene and that, conversely, non-Orientals with a low incidence of atypical ADH may be more at risk for alcoholism than are Orientals.

Familial Alcoholism

Jellinek and Jolliffe (1940) proposed a diagnostic category called "familial alcoholism." The Danish studies, in particular, seem to support this concept. Familial alcoholism, as described by Jellinek and supported by the Danish data, consists of the following features.

1. A family history of severe, unequivocal alcoholism
2. Early onset
3. Binge-type drinking patterns, requiring treatment at a relatively young age
4. No increased susceptibility to other types of substance abuse or diagnosable psychiatric illness.

From a research standpoint, separating "familial" from "nonfamilial" alcoholism may reveal some interesting and useful correlations. About half the alcoholic patients on many alcoholism wards give a family history of alcoholism. Thus, separating alcoholic patients into these groups would yield similarly sized cells for comparison purposes.

One study (Lucerno et al. 1971) found that if alcoholics had one alcoholic family member, 82 percent of them reported having two or more family members who were alcoholic, further strengthening the concept of familial alcoholism.

Another study (Parker 1972) found that 69 percent of women alcoholics who were "spree" drinkers, as opposed to 22 percent of women alcoholics who were "nonspree" drinkers, had fathers who were heavy drinkers. As Cotton (1979) pointed out, many additional variables, such as age of onset of heavy drinking, the interval between the first drink and heavy drinking, the efficacy of different treatment modalities, or the frequency of marriage to an alcoholic spouse, may differentiate alcoholics who have a family history of alcoholism from those who do not.

Summary

In this review of family histories of male and female alcoholics, the following can be concluded: Alcoholism occurs more often in male than in female relatives of alcoholics; more often in the families of women alcoholics than in those of men alcoholics; and more often in near rather than distant relatives. Alcoholism occurs more frequently than do other mental illnesses in families of alcoholics. Depression, the most often reported overlapping illness with alcoholism in families, still occurs much less frequently than does alcoholism.

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WOMEN ALCOHOLICS: A COMPARISON OF THE NATURAL HISTORY OF ALCOHOLISM BETWEEN MEN AND WOMEN* †

Michie N. Hesselbrock

Introduction

The number of studies focusing on alcoholic women has been increasing within the last few years, but a limiting factor in this research is the problem of identifying the large number of women known to be alcoholics. As the number of women who seek treatment for alcoholism increases, the need for knowledge about them becomes crucial. This paper thus examines male-female differences in a sample of alcoholics in terms of demography, psychopathology, and chronology of events leading to treatment for alcoholism.

Studies of demographic differences between male and female alcoholics have thus far been inconclusive. Lisansky (1957) found that men and women in an outpatient clinic for alcoholics were similar in terms of socioeconomic background, age, education, and religious affiliation. However, lower socioeconomic status female alcoholics (on a State farm) were different from men and women

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* This work was supported by grant 1-P50 AA 03510-03 from the National Institute on Alcohol Abuse and Alcoholism.

†The author wishes to express her thanks to Ms. S. Sposato, M. Weidenman, and K. Workman for collecting data and Drs. R. Meyer, H. Tennen, and V. Hesselbrock for helpful comments.

outpatients with regard to the above-mentioned variables, suggesting that socioeconomic factors, rather than gender per se, account for these differences.

Another study (Hoffman and Noem 1975) found that more female than male alcoholics were high school graduates. However, when dealing with demographic variables, we cannot single out any one factor to the exclusion of others. Socioeconomic status may be affected by education, age, and employment patterns. Factors such as employment influence drinking patterns (Horn and Wanberg 1971), and the differential impact of employment on men and women must be considered. Likewise, the rapidly changing role of women in our society has affected employment patterns, and it seems important to determine how these changes are reflected in a current population of female alcoholics.

Research into the childhoods of alcoholics suggests that, as children, male alcoholics tend to be more antisocial and have more school problems than female alcoholics (Rimmer et al. 1971; Schuckit and Morrissey 1976), but findings regarding the parents of alcoholic men and women are more equivocal. Lisansky (1957) and Bromet and Moos (1976) found that more female alcoholics reported parents (especially fathers) with drinking problems, but Sclare (1976) reported that more male alcoholics have fathers with drinking problems. These conflicting results could reflect sampling differences; the sample of alcoholics for the former came from the United States, while the latter were from England. In addition, blacks were excluded from Lisansky's population, and there was no mention of such exclusion in other studies. Additionally, conflicting reports about parents of alcoholics may have resulted from variations in the way the problem was defined. None of the above-mentioned studies made clear their definition of "alcoholism."

Variability in the diagnosis of alcoholism and in the definition of psychopathology has contributed to the confusion and to the popular belief that alcoholic women are more psychiatrically ill than alcoholic men are. The use of more reliable definitions of psychiatric illness will help establish whether psychiatric problems precede alcoholism more often in women than in men, or whether women suffer more psychiatric problems as a result of their drinking problems.

The age of first drink varies from study to study, but there is general agreement that men start drinking at an earlier age than women, regardless of other demographic factors (Lisansky 1957; Rimmer et al. 1971; Elder 1973; Beckman 1975; Goodwin 1976).

Furthermore, women start regular drinking later than men, but they tend to come to treatment facilities at a younger age than do men (Beckman 1976) indicating more rapid progression from regular drinking to alcoholism. It is not known, however, what process takes place in the intervals between the first drink to the first regular drinking and then to the loss of control. The study of the life history of alcoholism may help identify crucial points in the progression so efforts can be directed toward prevention and early intervention.

While alcoholic women have been found to be heterogeneous and the need for identifying subtypes within the female population is great, this study will limit itself to a comparison of sex differences using preliminary data available.

Methodology

The study sample was drawn from a 21-day inpatient alcohol treatment unit at the University of Connecticut Health Center. On admission, all patients were asked to fill out a demography form, including indicators of childhood adjustment and family background. At the end of the admission day, randomly selected patients were given a brochure, an explanation of the research procedure, and asked to participate. The following day, those patients who volunteered began filling out questionnaires, having interviews, and spending several afternoons in research activities. Data were collected on their alcohol and drug use history, personality characteristics and social-psychological adjustment, and symptom patterns. In addition, a neuropsychological assessment, using the Halstead-Reitan test, an EEG, and a biomedical evaluation, was conducted on each research patient. A comprehensive psychiatric interview was conducted by a trained staff member using the NIMH Diagnostic Interview Schedule (Robins et al. 1979). Psychiatric diagnosis lifetime was made based on Feighner's (1972) criteria. An additional interview was conducted to collect data on the chronology of events leading to alcoholism. Analyses of demographic information, psychiatric diagnoses, and chronology of alcoholism were performed on these preliminary data of 54 patients who were treated between January and August 1979. All but 2 (a man and a woman) were diagnosed as "definite" alcoholics according to the Feighner criteria (Feighner et al. 1972). The remaining 2 were diagnosed as "probable" alcoholics.

Description of the Sample

Demographic information on the study sample is described in table 1. The first 54 patients included 30 males and 24 females. The mean age of the women was slightly lower than that of the men (36 and 40 years old, respectively), but the difference is not statistically significant. The sample was predominantly white. Most were Catholic (72 percent of the men and 83 percent of the women). More than one-third of the men and women were married and living with their spouses (38 percent and 42 percent, respectively). Separation and divorce were more frequent among men than women (38 percent versus 21 percent). Most of the patients were high school graduates or had higher education. Only 24 percent of the men and 12 percent of the women did not finish high school. Almost one-third of the sample owned their houses; one-half of the sample rented houses or apartments. The majority of both men and women maintained their own households. Only 14 percent of the men, but 25 percent of the women lived with parents, relatives, or friends. The demographic variables examined thus far indicate no significant differences by sex, but men and women alcoholics did differ significantly in terms of employment status and source of income. Most men (72 percent) in the sample worked full-time at the time of admission, but only 25 percent of the women were employed full-time. Furthermore, half of the women who were not working outside their homes reported that they had not worked full-time for at least 4 years. Consequently, although most men indicated their job as a main source of income (75 percent), only one-third (29 percent) of the women reported that to be the case. Nearly half of the women who were not working reported their spouse as their main source of income. Significantly more women (41 percent) than men (18 percent) received public assistance and/or disability pensions.

Family background and childhood behavior problems are shown in table 2. Most men and women grew up in intact families. The women in the sample tended to have an alcoholic father (63 percent), while 48 percent of the men reported an alcoholic father. Men tended to have more behavioral problems in their childhoods

Table 1. Demographic Descriptions of Male and Female Alcoholics

Characteristic	Male (N=30)	Female (N=24)	Total (N=54)
Ethnic background	%	%	%
Black	14	8	11
White	86	92	89
Irish	21	12	17
European	31	33	32
Other	34	47	40
Religion			
Catholic	72	83	77
Protestant	21	17	19
Other/None	7	0	4
Education			
Less than high school	24	12	19
High school / GED	35	50	41
Some college	24	25	25
College degree	27	13	15
Legal marital status			
Single	24	29	26
Married and live together	38	42	40
Separated or divorced	38	21	30
Widowed	0	8	4
Residential arrangement			
Own home	27	29	28
Rent house or apartment	59	46	53
Live with parents, relative, or friends	14	25	19
Employed full-time			
Yes	72	25	51
No	28	75	*49
Last full-time job held			
1-6 months ago	17	21	19
6 months to 4 years ago	7	12	9
More than 4 years ago	4	42	21
Source of income			
Job	75	29	54
Spouse	7	29	17
Public assistance/disability	18	41	**29
Mean age at the time of admission	40	36	38
Standard deviation	12	10	11
Mean age at first marriage	25	21	23
Standard deviation	6	2	5

* P<0.001

** P<0.001

than the women. They were more often truant, aggressive, and had been arrested as juveniles.

Table 2. Family Background and Childhood Behavior of Male and Female Alcoholics

Background and Behavior	Male (N=29)	Female (N=24)	Total (N=53)
Family			
Both parents present until age 16	62%	75%	68%
Mother had alcohol problem	14	21	17
Father had alcohol problem	48	63	55
Childhood Behavior Problem			
Juvenile arrest	21	12	17
Treated for behavioral or emotional problem before 18	18	17	17
Fought a lot	44	27	37
Problem with stealing	19	18	18
Overly aggressive	30	18	25
Truant	22	9	16

Psychiatric Problems and Treatment Experiences

The subclassification of male and female alcoholics by onset of psychiatric diagnosis is shown in table 3. The proportion of primary alcoholism among men and women is similar. In this sample, nearly half of both men and women had other psychiatric diagnoses before they developed alcoholism. The most common initial diagnosis was antisocial personality. When alcoholism was not preceded by another psychiatric illness, the risk of developing additional psychiatric illness seems low. Only 13 percent of the men and 4 percent of the women developed depression or drug addiction after the onset of alcoholism.

Table 3. Subclassification of Alcoholics* by Onset of Psychiatric Diagnosis (NIMH-DIS) and Sex**

Subclassification	Male (N=30)	Female (N=24)	Total (N=54)
Primary alcoholism	43%	37%	41%
No other diagnosis	30	33	32
Developed depression or drug addiction later	13	4	9
Alcoholism secondary to other psychiatric diagnosis	57	63	59
Preceded by antisocial personality	47	37	43
Preceded by depression	7	13	9
Preceded by drug addiction	3	13	7

*Includes one male and one female who were diagnosed as probable alcoholics by NIMH-DIS.

**NIMH-DIS - Diagnostic Interview Schedule (Robins et al. 1979), Diagnoses made according to Feighner et al. criteria (1972).

Table 4 indicates the three most common psychiatric diagnoses among the alcoholic sample. Antisocial personality was the most frequent diagnosis for men (47 percent); drug dependence was most common (54 percent) for women. Drug dependence was found in twice as many women as men. Many women who were diagnosed as drug dependent became addicted to tranquilizers prescribed by physicians. The combined rates of antisocial personality and depression are similar for men and women. However, totaling the number of psychiatric diagnoses (antisocial personality, drug dependence, depression), women showed more problems than men. One-third of the men, but more than one-half of the women had three or more psychiatric diagnoses. However, this difference is only marginally significant. Another indication that women in this sample may have more psychopathology is that significantly more women than men were treated for psychiatric problems other than alcoholism. Almost 90 percent of the women but only 52 percent of the men were treated for psychiatric problems.

Table 4. Psychiatric Problem and Treatment Among Male and Female Alcoholics

Diagnosis	Male (N=30)	Female (N=24)	Total (N=54)
Additional psychiatric diagnosis			
Antisocial personality	47%	42%	44%
Drug dependence	27	54	39
Depression	40	46	42
Alcoholism only	30	33	31
Number of psychiatric diagnoses			
1	30	33	31
2	40	13	28
3 or more	30	54	41
Treated for psychiatric problem other than alcoholism since age 18	52	88**	67

*% for psychiatric diagnoses does not equal 100 percent because some patients have multiple diagnoses.

**The male/female ratio is significant at 0.001 level.

There was very little difference between men and women in terms of previous treatment for alcoholism (table 5). For more than half of the men (52 percent) and for nearly half of the women (42 percent) the hospitalization studied in this research project was the first treatment experience. However, for nearly one-third of the sample (28 percent), this admission was at least the third treatment experience.

Men tended to schedule their admissions in advance, but twice as many women came to the treatment center directly from a detoxification center, indicating that the route to inpatient treatment for women may be more traumatic than for men.

Chronology of Alcoholism

Table 5. Treatment Experience for Alcoholism

Treatment	Male (N=29)	Female (N=24)	Total (N=53)
Admitted directly from a detoxification center			
Yes	22%	42%	31%
No	78	58	69
Previous treatment for alcoholism before this admission			
Never	52	42	47
Once or twice	24	25	25
Three or more	24	33	28
Goal for treatment			
Stop drinking completely	96	87	92
Cut down	4	13	8

The development of a drinking problem from the time of the first drink to the first treatment experience is shown in figure 1. Both men and women in our sample took their first drink at early ages (14.1 and 14.8, respectively). The ages at first drink and at first intoxication are similar for men and women, but the women in this sample started to drink regularly (once a week or more) later than men (ages 19.5 for women and 17.9 years for men). Most men realized that alcohol relaxed them only after becoming intoxicated regularly for 3½ years, but most women recognized this effect earlier, even before establishing regular patterns of drunkenness. When women began to get intoxicated regularly, they seemed to progress to alcoholism more rapidly than men. Women were more likely to try to stop drinking sooner than men; and when they were unable to stop, quickly realized that they had alcohol problems. It is noteworthy that the women's realization that they had drinking problems corresponded both to the time that they first tried to stop drinking and to the times their family/friends first confronted them with their problems. However, most women waited an average of 3 years before seeking treatment.

The chronology of events of alcoholism for men covers a longer period of time than that for women. For men, the age of regular drinking corresponded with the age of first intoxication. However, the progression from regular drinking to the time they sought treatment was longer than that of women. Unlike women, men usually did not stop drinking until a family member or friend expressed concern about their drinking. Eventually, the men tried to stop and quickly discovered that they had alcohol problems. A longer time elapsed, however, between recognition of the problem and a search for treatment.

Figure 2 shows the time elapsed between phases of the drinking problem. Women progressed more slowly than men from their first drink to regular drinking and from first drink to regular intoxication. However, when women begin to get drunk regularly, they seem to progress to problem drinking much faster than men. Both men and women seem to recognize their drinking problems within a year of their initial attempt to stop drinking, but women progress to that point sooner than men and seek treatment sooner than men. Unlike women, men do not try to stop their drinking until 3½ years after the family mentions the problem. Even after recognition of their drinking problems, men tend to wait several years before they seek treatment.

Summary and Discussion

In summary, no demographic variables distinguished between men and women alcoholics in this sample except employment. Nearly half of the women who did not work were housewives. But the role of women in this country has been rapidly changing, and role conflict is considered a contributing factor to alcoholism (Parker 1972; Scida and Vannicelli 1979). So future research should investigate whether women alcoholics should be subclassified by employment status. Furthermore, the interrelatedness of various demographic factors, such as age, employment, socioeconomic status, and educational achievement must be investigated. The male alcoholics in this study tended to be more antisocial in childhood than the female alcoholics. Although this finding is consistent with previous research (Rimmer et al. 1971; Schuckit and Morrissey 1976), further exploration of the differential effect of parents' socioeconomic status and behavior, especially antisocial behavior, on later adjustment is necessary.

In this sample, more female than male alcoholics had a parent with an alcohol problem. This finding is consistent with the findings of Lisansky (1975) and those of Bromet and Moos (1976). The alcoholic men and women in this sample were similar in terms of primary and secondary alcoholism. However, there was some indication that the women alcoholics may have been more psychiatrically ill. The women generally had more psychiatric problems than the men and had more treatment for psychiatric problems in their adult lives. These results substantiate previous findings (Rimmer et al. 1971; Beckman 1975; Beckman 1976; Schuckit and Morrissey 1979) indicating more severe psychopathology among women than among men alcoholics.

The women in this study seemed to begin drinking regularly at a later age than the men, but the mean age of the first drink is comparable for men and women. This finding differs from previous reports. For example, Elder (1973), in a study of sober female Alcoholics Anonymous members in the Midwest, found that they took their first drinks at age 17. Rimmer et al. (1971) reports a similar age for first drink among women admitted to a psychiatric hospital for alcohol problems. This sample was small; therefore, this finding, controlling for demographic factors in a larger sample of women, must be investigated.

The finding that women, unlike men, began regular drinking after realizing alcohol gave relief is consistent with previous findings suggesting that women tend to drink to forget stressful experiences in their lives or use alcohol to self-medicate (Schuckit 1973; Beckman 1975; Gomberg 1976). In addition, women may be more self-conscious about their drinking. They recognized their problems with alcohol at the same time that a friend or another family member did. Male alcoholics, on the other hand, did not admit their drinking problems until a few years after their families or friends mentioned the problem to them. This finding indicates different cultural influences on men and women in our society. Our culture is generally more permissive toward men's drinking heavily and becoming intoxicated; women are still stigmatized for such behavior.

It is interesting that neither men nor women recognized their own drinking problems until they attempted to stop drinking. This finding seems to support the notion that many problem drinkers do not admit their alcohol problems and that one of the first steps in treatment is to help alcoholics accept the reality of their alcohol problems.

It is generally believed that women seek help for illness (physical as well as psychiatric) more often than men. Men's reluctance to seek treatment for their alcohol problems is reflected in the longer time between the discovery of their problems and their first treatment experiences.

In conclusion, while the number of men and women in the sample is small, the findings address various issues and theories in the research of differences between men and women alcoholics. While men and women alcoholics in the sample are similar in terms of demographic background, major differences were found in the natural history of alcoholism. While women had a later onset of regular drinking and intoxication than men, once they began intoxicating regularly they progressed to having a drinking problem much sooner than men. However, factors which may contribute to these differences must be studied in a larger sample of men and women alcoholics. Further data will be collected on the sample, with the intention of providing more definitive answers to these questions in the near future.

Figure 1. Chronology of Alcoholism Among Men and Women

	Men (N=29)	Women (N=24)
	14.1-First Drink	14.8-First Drink
15 Yrs.	17.8-First Drunk 17.9-Regular Drinking	17.9-First Drunk 19.5-Regular Drinking
20 Yrs.	21.8-Getting Drunk Regularly	23.8-First Realized Alcohol Gave Relief
25 Yrs.	25.3-First Realized Alcohol Gave Relief	25.6-Getting Drunk Regularly 29.7-First Tried to Stop
30 Yrs.	30.2-Family/Friends Said Had Drinking Problem 32.0-First Tried to Stop 32.8-First Realized Had Drinking Problem	30.0-Family/Friends Said Had Drinking Problem -First Realized Had Drinking Problem 33.0-First Treatment
35 Yrs.	38.0-First Treatment	
40 Yrs.		

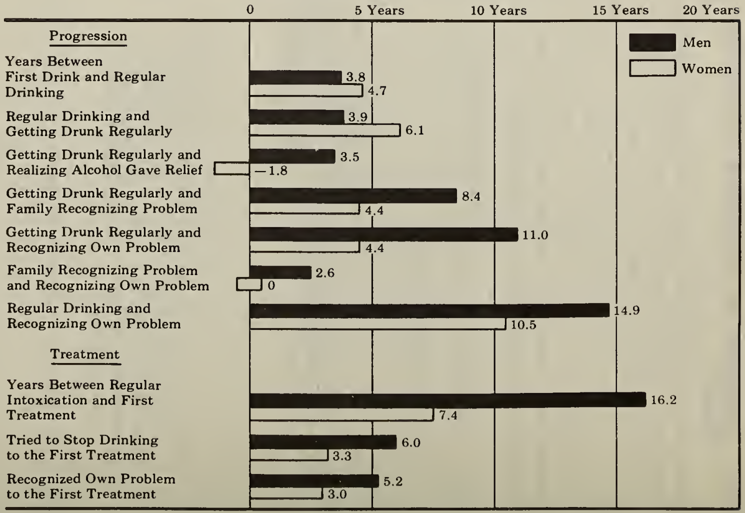

Figure 2. Years Between Stages of Alcoholism

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SOME RECENT FINDINGS IN THE STUDY OF GENOTYPE-ENVIRONMENT INTERACTION IN ALCOHOLISM*

Theodore Reich, C. Robert Cloninger, Collins Lewis, and John Rice

Introduction

Several large-scale family studies such as the one by Winokur and his colleagues in the late 1960s have established that alcoholism is a strongly familial disorder. In addition, men in the general population and in the families of alcoholic probands had a much higher risk than women. Schuckit et al. (1972) studied the half-sibs of alcoholic probands and demonstrated that alcoholism could be transmitted from parent to offspring, even when not raised by an alcoholic biologic parent. These data were interpreted as supporting the existence of a genetic factor in the etiology of alcoholism.

Goodwin et al. (1973) studied the adopted-away sons and daughters of alcoholic male probands in Denmark and established that alcoholism can be transmitted from father to son, even if the child is given up for adoption early in life. A recent replication by Bohman (1978) makes this finding even more certain. Both these studies strongly support the view that genetic factors are of etiologic importance in the development of alcoholism.

A survey of the cultural patterns relevant to heavy drinking and alcoholism indicates that nongenetic environmental and cultural

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* This work was supported in part by grants AA-03539, MH-31302, MH-25430, and MH-00048 from the U.S. Public Health Service.

factors are also important. Current etiologic theories must therefore take into account both genetic and nongenetic factors in alcoholism. Indeed, both types of factors are so closely entwined that an understanding of one cannot proceed without an understanding of the other.

To clarify the gene-environment interaction in alcoholism, a large-scale family study of alcoholism was conducted (Principal Investigator, C. Robert Cloninger). This report presents preliminary results concerning gene-environment interaction.

A Family Study of Alcoholism

A random sample of white male and female subjects was chosen from three psychiatric inpatient units of the Department of Psychiatry of Washington University in St. Louis. Subjects were obtained also from a county parole office. Each subject participated in a structured interview of known reliability, the Home Environment and Lifetime Psychiatric Experience Record (HELPER) (Coryell et al. 1978), and received a psychiatric diagnosis based on Feighner et al. (1972) criteria. Subjects received a diagnosis of either "no alcoholism," "probable alcoholism" (symptoms in two groups), or "definite alcoholism" (three or more symptoms in three groups). For this report we chose all 131 alcoholic probands from the first 150 completed families (74 probands from the inpatient population and 57 from the parole office sample). Thirty-two age- and sex-matched "control probands" were selected who were medically or surgically ill inpatients, not diagnosed as psychiatrically ill by interview.

All current or most recent spouses and all first-degree relatives were contacted and approximately 70 percent of those who resided within a 100-mile radius of St. Louis were personally interviewed. Each relative was evaluated by a structured psychiatric interview, a battery of psychological personality tests, and a schedule to measure relevant rearing experiences. A family history was obtained from each relative; using these data as well as hospital and other records, diagnoses were assigned to both interviewed and noninterviewed individuals. Two psychiatrists made the diagnoses and contradictions were resolved by consensus. The study is still in progress.

Table 1 shows the percentage of prevalence of probable and definite alcoholism in the relatives of probands. As with the earlier study (Winokur et al. 1970), it can be seen that male relatives are affected much more frequently than are female relatives and that the relatives of male and female probands have almost the same sex-specific prevalences.

The prevalence of probable and definite alcoholism in the relatives of male and female control probands is given. Approximately 4 percent of the female first-degree relatives (123 sample) and 20 percent of the male first-degree relatives (132 sample) were alcoholics. Of 64 grandfathers studied, 5 percent were alcoholics. It is clear from these data that alcoholism is strongly familial.

Table 2 shows correlations between relatives obtained by fitting a multifactorial model to the entire data set. They illustrate that alcoholism is extremely familial. The correlation between fathers and sons ($r_{poMM} = 0.50$) and the correlation between mothers and daughters ($r_{poFF} = 0.31$) are similar to those obtained during the earlier family study. The population prevalence figures ($K_{pM} = 0.20$ for males and $K_{pF} = 0.056$ for females) are higher than earlier population prevalences. Since this study used a different instrument and a different method of ascertainment, it is not clear if the difference between these and earlier figures is real or is artifactual. The correlation between sibs (r_{oo}) is very high, and these correlations are similar to those obtained in an earlier study. The correlation between mates ($m = 0.52$) is also very high and indicates that a great deal of assortative mating for alcoholism has occurred. That alcoholism may be transmitted over three generations is seen by the value of the correlations between grandfathers and grandsons ($4_{GoMM} = 0.32$).

Assortative Mating

Three types of assortative mating might occur in a disorder such as alcoholism. One type may be termed "social homogamy," in which individuals mate because they belong to a specific socioeconomic class or group. These individuals may not manifest alcoholism or even heavy drinking when they mate. In a second type of assortative mating termed "direct phenotypic assortative mating," individuals mate because each has an excessive liability to develop alcoholism. The third kind of assortative mating called "contagion"

Table 1. Prevalence Percentage of Alcoholism in Relatives of Alcoholic Probands (total numbers of observations in parentheses)

Alcoholic Probands	RELATIVES					
	Fathers	Mothers	Brothers	Sisters	Grandfathers	Spouses
Male (103)	47%(102)	20%(102)	62%(109)	12%(100)	16%(196)	18%(38)
Female (27)	48 (27)	15 (27)	56 (25)	21 (34)	4 (50)	39 (23)
Total (130)	47 (129)	19 (129)	61 (134)	14 (134)	11 (246)	26 (61)

occurs when an alcoholic spouse induces a mate to drink excessively and become alcoholic.

Table 2. Correlations Between Relatives Obtained by Fitting an Unrestricted General Multifactorial Model to the Entire Data Set

$r_{poMM} = 0.50 \pm 0.09$

$r_{poMF} = 0.38 \pm 0.10$

$r_{poFM} = 0.46 \pm 0.12$

$r_{poFF} = 0.31 \pm 0.13$

$K_{pM} = 0.20 \pm 0.03$

$K_{pF} = 0.056 \pm 0.01$

$r_{ooMM} = 0.60 \pm 0.08$

$r_{ooMF} = r_{ooFM} = 0.41 \pm 0.10$

$r_{ooFF} = 0.48 \pm 0.13$

$m = 0.52 + 0.08$

$r_{GoMM} = 0.32 + 0.12$

In a recent study which used both path analysis and segregation analysis of family data in alcoholism, the pattern of direct phenotypic assortative mating fitted the data rather well. The possibility that social homogamy also had occurred was not tested. A second statistical test was performed to find out whether the presence of alcoholism in the spouse of an alcoholic proband influenced the transmission of alcoholism to the offspring. The test results were highly significant, and indicated that the affected spouse strongly added to the transmissible elements. The authors are now developing models to determine whether the alcoholism in the spouse of an alcoholic proband is the consequence of contagion or of direct phenotypic assortative mating. A model is also being developed which will test for all three types of assortative mating patterns and will enable the authors to determine the relative occurrence of each of the three types of patterns.

The Transmission of Severity

The possibility that severity of alcoholism is transmitted in families was tested by comparing the families of male and female alcoholics with "definite" alcoholism (symptoms in three or more groups) with probands who had "probable" alcoholism (symptoms in two groups) using explicit criteria of Feighner et al. (1972). As table 3 shows, the family distribution of probable and definite alcoholism was no different in the families of the definite or probable alcoholic probands. From this, it is concluded that severity measured in this fashion is not transmissible and may be due to the interaction between a tendency toward alcoholism and nonfamilial environmental factors.

Relationship to Antisocial Personality

Individuals with antisocial personalities have been reported to develop alcoholism at an unusually high rate. This association has led some writers to group antisocial personality and alcoholism into the category of personality disorders rather than to separate them into two independent illnesses. In table 4, the prevalences of alcoholism and antisocial personality in the first-degree relatives of male probands with alcoholism and antisocial personality are compared.

The relatives of probands with only alcoholism or only antisocial personality (ASP) are at increased risk only for the same illness as their related probands. That is: the frequency of alcoholism in the families of probands who have only alcoholism is elevated above the population prevalence, and the frequency of ASP in the families of probands who have only ASP is also elevated above the population prevalence. The largest group, in which the probands have both alcoholism and antisocial personality, shows an increased family prevalence for both disorders. Indeed, the risk for alcoholism in the first-degree relatives of individuals with alcoholism and antisocial personality is elevated above the risk for alcoholism in the first-degree relatives of alcoholics who are not also diagnosable as having antisocial personalities. The implication is that alcoholism and antisocial personality are independent disorders and are not necessarily transmitted in the same families. The presence of antisocial personality in a family elevates the familial risk of alcoholism. It seems clear that there is some synergistic interaction between antisocial personality and alcoholism, a hypothesis that was explored by analyzing data pertaining to sex effect and heavy drinking.

Table 3. Alcoholism in the First-Degree Relatives of Alcoholic Probands With Respect to Sex and Severity

	DEFINITE ALCOHOLISM				PROBABLE ALCOHOLISM	
Sex and Severity in Relatives	Female Probands (N = 26)		Male Probands (N = 93)		Male Probands* (N = 10)	
	f/n	Percent	f/n	Percent	f/n	Percent
Mothers and Sisters						
Definite alcoholic	$\frac{8}{68}$	12%	$\frac{22}{237}$	9%	$\frac{2}{26}$	7.6%
Probable alcoholic	$\frac{2}{68}$	3	$\frac{14}{237}$	6	$\frac{2}{26}$	7.6
Total	$\frac{10}{68}$	15	$\frac{36}{237}$	15	$\frac{4}{26}$	15
Fathers and Brothers						
Definite alcoholic	$\frac{27}{61}$	44	$\frac{96}{236}$	41	$\frac{8}{20}$	40
Probable alcoholic	$\frac{4}{61}$	7	$\frac{29}{236}$	12	$\frac{1}{20}$	5
Total	$\frac{31}{61}$	51	$\frac{125}{236}$	53	$\frac{9}{20}$	45

*No probable female alcoholic probands were observed.

Sex Effect and Heavy Drinking

Analyzing an earlier data set, Reich et al. (1975) and Cloninger et al. (1978; Cloninger, Reich, and Wetzel 1979) concluded that the preponderance of alcoholism in males could be explained entirely by nonfamilial environmental effects. Neither transmissible cultural nor genetic effects were required. In a recent analysis, Reich et al. (1979) used path and segregation analyses to test this hypothesis and again concluded that the sex effect in alcoholism could be due entirely to nonfamilial effects. The most likely candidate seemed to be "adequate exposure to heavy drinking." The difference between the frequencies of alcoholism in males and females would disappear both in the general population and in alcoholic families if females were exposed to the stimulus of heavy drinking. Termed the "environmental hypothesis," this conclusion was based on the observation that the families of male and female alcoholics were no different in terms of the prevalence of alcoholism in their male and female first-degree relatives. The present data set also supports this conclusion (table 1).

Tables 5, 6, and 7 show the results of testing the hypothesis that the relative deficiency of alcoholism in females is the consequence of their relatively low exposure to alcohol. Only interviewed first-degree relatives of probands with definite alcoholism were used to test this hypothesis. The relatives of male and female probands were combined because they did not behave differently and because the sample of females with antisocial personality was rather small.

As table 5 illustrates, the risk of definite alcoholism is higher in male than female relatives, and this effect is amplified if the relative also exhibits an antisocial personality. The results are statistically significant. Table 6 shows the same comparison by estimating the risk of heavy drinking in the interviewed first-degree relatives of definite alcoholics according to sex and diagnosis of antisocial personality in those relatives. Heavy drinking "is defined by, having a history of a daily consumption of 2 or more drinks, or more than 3 drinks per day for 3 or more days per week, or being drunk 12 or more times per year." Table 6 shows that the sex effect is maintained in the male and female relatives of alcoholics with and without antisocial personalities. A remarkable 98 percent of the male relatives with antisocial personality also drink heavily. The results are statistically significant. These data support the idea that the sex effect, as described, persists and is even amplified.

In table 7, the risk of definite alcoholism is computed as in table 6. However, the duration of heavy drinking is "controlled for" in terms of the proportion of the subjects' lifetime during which they are at risk for alcoholism. The morbid risk for alcoholism is thus calculated per unit of time of heavy drinking. This table shows that the morbid risk for women without antisocial personality is 37 percent and that for men it is 44 percent. The difference is not significant. When the relative had an antisocial personality, the risk to women is 61 percent, and the risk for men, 81 percent. Again, the difference is not significant.

These data (tables 5, 6, and 7) confirm the hypothesis that the risk to women and men for alcoholism is very similar if the duration and amount of heavy drinking is controlled. Thus, if the frequency, duration, and volume of drinking among women increase, the sex effect for alcoholism should disappear. In that case, the population prevalence for alcoholism should become the same in males and females, and the risk to male and female relatives of alcoholic probands should also be the same.

The data in tables 5, 6, and 7 also support the view that antisocial personality is a powerful factor, increasing in an interactive way both the frequency of heavy drinking and the proportion of heavy drinkers who become alcoholics.

Family Structure

Woodruff et al. (1972) showed that alcoholism is one of the psychiatric diagnoses most closely associated with divorce. Divorce itself tends to run in families, and it may be that family structure (whether or not an individual comes from a broken home) may also be familial and that in some kindreds this characteristic is related to alcoholism. These hypotheses were tested, and the results appear in tables 8 and 9.

Table 8 shows the family structure of 50 felons. These individuals averaged 21.6 years of age, and it is clear from the table that most were reared in unstable homes. Only 54 percent of the subjects were reared in a home by a stable mother and father from ages 0 to 15, and, although 22 percent lived at least 6 months with a single parent of rearing, none of them lived with the same single parent of rearing from ages 0 to 15.

Table 9 displays the structure of the families of 50 alcoholic patients, with an average age of 41 years. At age 15, only a minority lived with their biological fathers and mothers, and from the ages of 0 to 15, only 40 percent did so. As before, no alcoholic raised for a significant period of time by a single parent was reared throughout the first 15 years by this same parent. These data support Woodruff's view (1972) that alcoholism is in some fashion related to divorce or at least to marital dissolution. There clearly seems to be an interaction between alcoholism and family structure (Reich et al. 1978).

The incorporation of family structure into models for the tramsmission of alcoholism between generations is difficult. Cloninger, Rice, and Reich (1979*a*, *b*) developed a general approach to dealing with this factor, but experience with practical applications is still needed, especially in cases of repeated divorce. The interaction of family structure in the presence or absence of alcoholism is poorly understood and requires additional research.

Some Biological Markers

Schuckit et al. (1979) looked at the clearance of blood aldehyde after a single dose of ethanol in a group of 20 healthy young nonalcoholic subjects—the offspring or siblings of alcoholics—and compared it with that of demographically matched controls with the same drinking history. Control group members had no alcoholic relatives. As shown in figure 1, the experimental subjects had statistically significant higher mean blood aldehyde concentrations. If this study can be replicated, the concentration may prove important in studying gene-environment interaction in alcoholism. Of course, some of the experimental subjects may be biologically at increased risk for alcoholism, and the environmental and cultural phenomena noted may trigger the disorder.

In another biological study, Blass and Gibson (1977) compared the transketolase activity in red blood cells from patients with Wernicke-Korsakoff syndrome to that of non-Wernicke-Korsakoff controls. As illustrated in figure 2, the controls had a higher activity level than the patients. The implication is that some individuals are differentially susceptible to low thiamine in their diets and that at least some Wernicke-Korsakoff syndrome may be the result of a thiamine-deficient individual's being challenged with a poor diet or a high consumption of alcohol. Again, gene-environment factors seem to be important in the etiology of this complication of alcoholism.

Many genetic marker studies have been performed in an attempt to detect association and linkage with alcoholism, but the results have been inconsistent, as one might anticipate with an etiologically heterogeneous phenotype. Conflicting reports of the association and linkage of alcoholism with color blindness, various blood groups, and other markers are reviewed by Hill et al. (1975) and Winokur et al. (1976). Tanna and Winokur in collaboration with Elston and Go (1976*a*, *b*; 1979) reported possible linkage of depressive spectrum disease with α-haptoglobin in 14 families. However, the absence of affective disorder in the adopted-away daughters of alcoholics (Goodwin et al. 1977) and the relative deficiency of alcoholism in the relatives of depressive probands (Cloninger, Reich, and Wetzel 1979; Cloninger, Rice, and Reich 1979*a*, *b*) cast doubt on this hypothesis. Independent replication on a larger scale is needed.

One observation that has been replicated independently is the association of nonsecretor status with alcoholism, particularly among the individuals of blood type A (Camps and Dodd 1967; Camps et al. 1969; Swinson and Madden 1973). Also, several recent studies of associations of HLA haplotypes reveal some interesting observations. Alcoholism in general is not associated with any particular haplotypes, but alcoholics with cirrhosis have been found to have an excess of HLA-B8 and a deficiency of HLA-A28, when compared with other alcoholics and with controls (Bailey et al. 1976). This finding indicates that specific complications of alcoholism may be associated with different predisposing genetic factors.

Discussion

Current thinking about complex genotype-environment disorders such as alcoholism is that both genetic and nongenetic relevant parameters must be taken into account to develop a model for the transmission of the disorder. The field of genetic epidemiology is moving quickly toward this goal, so that various models, genetic effects, environmental effects, and interactions can be demonstrated.

This paper attempted to illustrate several important kinds of genotype-environment interactions, including sex effect, severity, assortative mating, heavy drinking, and the interaction between one disorder and a second disorder correlated with the first. Problems arising from family structure were also discussed.

Understanding genotype-environment interactions would be greatly facilitated if relevant biological substrates could be found. If it were possible to biologically detect susceptible individuals, discovery and specification of cultural or environmental effects leading to the development of the disorder in these individuals would be greatly simplified. This report considers available biological markers. Replication of these results will lead to a more comprehensive model of the gene-environment interaction in the development of alcoholism.

Cloninger et al. (1978; Cloninger, Reich, and Wetzel 1979) have suggested several hypotheses that need to be tested on a larger data set. These are: (1) frequency of drinking is transmitted independently of predisposition to alcohol dependence and is predominantly determined by nongenetic factors; (2) frequent heavy drinking is largely a sex-typed sociocultural phenomenon, and prealcoholic psychopathology or social stress may precipitate it; and (3) predisposition to alcohol dependence is largely a genetic phenomenon (and independent of a genetic predisposition to antisocial personality), but continued heavy drinking is required before the predisposition manifests itself.

Table 4. Alcoholism and Antisocial Personality in All First-Degree Relatives* of Male Probands With Alcoholism and With Alcoholism Plus Antisocial Personality**

	Diagnoses in Relatives							
	Female				Male			
	Alcoholism		Antisocial Personality		Alcoholism		Antisocial Personality	
Probands Diagnoses	Freq.	Pct.	Freq.	Pct.	Freq.	Pct.	Freq.	Pct.
Alcoholism only (N = 31)	3/70	4%	1/70	1%	22/67	33%	2/67	3[a]
Alcoholism plus antisocial personality (N = 48)[b]	16/136	12	4/136	3	60/131	46	22/131	17[a]
Antisocial personality only (N=7)	0/13	0	1/13	8	1/17	6	3/17	18

[a] $p < 0.01$ by X^2 test.

[b] One adopted proband was omitted because no information could be obtained about his first-degree relatives.

*Only parents and siblings were included since the number of children who had reached the ages risk was inadequate for analysis.

**All diagnoses are at the definite level.

Table 5. **Risk of Definite Alcoholism in Interviewed First-Degree Relatives of Definite Alcoholics According to Sex and Diagnosis of Antisocial Personality (ASP) of Relative**

ASP in Relative	Sex of Relative: Woman A/N	%	Men A/N	%
Not ASP	14/143	10%*	25/84	31%
ASP	4/12	33**	37/50	74

*$p < 0.01$ by X^2 on 10% versus 31%.

**$p < 0.01$ by X^2 on 33% versus 74%.

Table 6. **Risk of Heavy Drinking (H) in the Interviewed First-Degree Relatives of Definite Alcoholics According to Sex and Diagnosis of Antisocial Personality (ASP) in the Relative**

ASP in Relative	Sex of Relative: Women H/N	%	Men H/N	%
Not ASP	49/143	34%*	65/84	77%
ASP	8/12	67**	49/50	98

*$p < 0.01$ by X^2 on 34% versus 77%.

**$p < 0.01$ by X^2 on 67% versus 98%.

Table 7. **Risk of Definite Alcoholism (A) in Interviewed First-Degree Relatives (N) of Alcoholic Probands, Adjusting for Duration of Heavy Drinking and Presence or Absence of Antisocial Personality* (ASP)**

	Sex of Relative					
	Women			Men		
ASP in Relative	N	A/BZ*	%	N	A/BZ	%
Not ASP	49	14/37.8	37	65	25/56.5	44
ASP	8	4/6.6	61	49	37/45.8	81

* BZ = "bezug ziffer" or number corrected to account for duration of heavy drinking in terms of proportion of lifetime morbid risk for alcoholism.

Sex differences are not significant ($p < 0.05$).

Table 8. Structure of Families of 50 Felons (mean age = 21 years)

		Number of Parents of Rearing				
		1		2		3+
Age						
At age 10	Mother	8%	Mother-Father	70%		
	Other	6	Other	12		
	Total	14	Total	81	Total	4%
At age 15	Mother	10	Mother-Father	68		
	Other	12	Other	16		
	Total	22	Total	74	Total	4
From 0-15			Mother-Father	54		
			Other	22		
	Total	0	Total	76	Total	24

Table 9. Structure of Families of 50 Alcoholic Patients (mean age = 41 years)

		Number of Parents of Rearing				
Ages		1		2		3+
At age 10	Mother	8%	Mother-Father	58%		
	Other	6	Other	16		
	Total	14	Total	74	Total	12
At age 15	Mother	12	Mother-Father	48		
	Other	16	Other	12		
	Total	28	Total	60	Total	12
From 0-15			Mother-Father	40		
			Other	18		
	Total	0	Total	58	Total	42

Figure 1. Mean Acetaldehyde Concentrations in Blood and Standard Errors of the Mean For Subjects and Controls After a Single Dose of Ethanol (0.5 mg/kg)

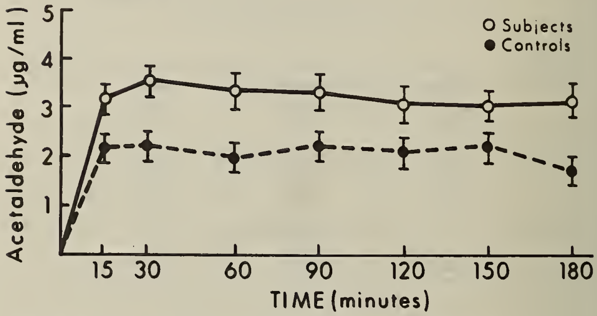

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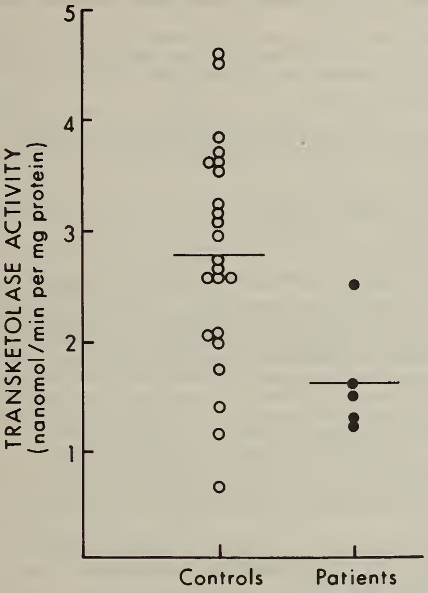
Figure 2. Transketolase Activity in Red Blood Cells From Patients With Wernicke-Korsakoff Syndrome and Controls



Transketolase activity was measured in lysed RBC from 5 patients with well-documented Wernicke-Korsakoff syndrome and 23 controls. At the time of this study, the patients had been treated with thiamine in hospital for at least 3 mos. The controls included 1 clinically normal individual and 22 patients on the wards of the Maudsley Hospital. Transketolase was measured by the spectrophotometric coupled-enzyme assay of Racker and coworkers in the presence of saturating (1 mM) thiamine pyrophosphate. Results were similar when expressed per mg hemoglobin instead of per mg protein. Reprinted with permission from Abnormality of a thiamine-requiring enzyme in patients with Wernicke-Korsakoff Syndrome. *The New England Journal of Medicine*, 297:1367-1370, 1977. Copyright 1977 by the Massachusetts Medical Society.

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MINIMAL BRAIN DYSFUNCTION AS AN ETIOLOGICAL PREDISPOSITION TO ALCOHOLISM

Ralph E. Tarter

Researchers and clinicians both generally agree that alcoholism is not a unitary disorder but, rather, is one that affects a heterogeneous population of individuals who are classifiable on the basis of personality traits (Goldstein and Linden 1969), drinking patterns (Wanberg et al. 1974), psychosocial history (Rudie and McGaughran 1961), and genetic-familial relationships (Goodwin 1971). Given the diversity of typologies, variously defined along biological, psychological, and social criteria, it is not surprising that current rehabilitation strategies and programs are far from effective, inasmuch as the critical treatment variables are masked by the heterogeneous characteristics that comprise the actual disorder. The factors affecting treatment outcome are still to be identified, as are the intrinsic characteristics of the alcoholic individuals of whom they are prognostic. Until the etiological and process variables can be classified into homogeneous categories, therapeutic efforts are bound to be both insufficient and ineffective.

As yet there is little consensus as to the best method to derive a classification system, but it would be heuristically and clinically relevant if the empirically derived categories contained uniform groups of individuals who exhibited distinct features across different levels of biological organization. Thus, the major objective is to develop criteria in which persons within one category demonstrate similar physiological, behavioral, and psychological characteristics, and individuals in another category exhibit qualitatively different characteristics in each of these areas.

One etiological risk factor associated with alcohol abuse and showing promise of identifying a subtype is hyperactivity (Tarter et al. 1977). "Hyperactivity" is often loosely applied to an array of behavioral problems, including restlessness, impulsivity, distractibility, lability, and aggressiveness, which are presumed to reflect a more fundamental disturbance in modulating arousal mechanisms. For some hyperactivity conditions, these mechanisms are theorized to have a genetic origin (Wender 1971). Neurochemical hypotheses have been proposed and specific treatment strategies recommended, to ameliorate both the hyperactivity and the frequently manifested psychological concomitants such as depression and anxiety. If such hyperactivity is antecedent to alcoholism, then it should have some bearing on the mode of treatment intervention.

With respect to alcoholism, early research findings have been very encouraging. Cantwell (1972) reported that, of children diagnosed as hyperactive, 10 percent had a parent who exhibited a similar disturbance. All of the parents of the hyperactive children had a psychiatric disorder, either sociopathy, alcoholism, or hysteria. Morrisson and Stewart (1973) found that hyperactive children were more likely to have an alcoholic parent than were a control group of children. Goodwin et al. (1975) reported that the biological children of alcoholics raised by surrogate parents had more hyperactive characteristics than did a control group of children. Mendelson et al. (1971) observed that 15 percent of hyperactive children were drinking excessively by the time they were 16 years old. Thus, there is some evidence indicating an association between childhood hyperactivity and alcoholism. However, because alcoholism itself is not a unitary condition (Winokur et al. 1971), it is not clear what the functional relationships are between childhood hyperactivity and adult drinking patterns. Therefore, one question concerns whether or not individuals exhibiting these antecedent characteristics, when compared with alcoholics without evidence of childhood hyperactivity, manifest differential alcoholism profiles.

Tarter et al. (1977) divided alcoholics into two groups based on severity of drinking excesses, and compared these with psychiatrically ill and normal groups on a number of familial, psychopathological, and childhood characteristics. Although the reports of childhood history of hyperactivity-minimal brain dysfunction (HK/MBD) were retrospective, striking differences were, nonetheless, observed between the groups. On a 50-item checklist, the more severe alcoholics endorsed a mean of 15.1 features frequently found in children with HK/MBD (Wender 1971), compared with a mean of 3.6 characteristics for the less severe alcoholics, and 3.4 characteristics for the normal controls. The latter two groups did not differ significantly from each other, but both reported significantly fewer HK/MBD characteristics than did the more severe drinkers. Thus, a differentiation among alcoholics was clearly obtained in which alcoholism severity, defined along clinical criteria, was found to be associated with a history of hyperactivity-minimal brain dysfunction. Moreover, the more severe drinkers scored significantly higher on the McAndrew Alcoholism Scale and the hypomania scale of the Minnesota Multiphasic Personality Inventory (MMPI) than the less severe drinkers did, indicating that the more severe drinkers are more energized, disinhibited, and exhibit more of the chronic features of alcoholism. In addition, the more severe alcoholics began their drinking careers at younger ages and reported becoming alcoholics earlier.

Of interest was the observation (Tarter et al. 1977) that the psychiatric group, consisting of patients with a mixture of neurotic disorders, also endorsed a high number of HK/MBD characteristics. Their overall score was 9.4 characteristics, but their scores were found to be largely affected by family history. Subjects with a family history of alcoholism reported a mean of 13.5 HK/MBD features, and the patients without such a history endorsed a mean of only 7.2 characteristics. Family history of alcoholism was found to be unrelated to the number of HK/MBD characteristics for the other three groups. Thus, alcoholism is not the only disorder consequential to HK/MBD; these factors also may precede other psychiatric disorders if there is a family history of alcoholism.

Another finding was that the less severe alcoholics resembled psychiatric patients; the most severe drinkers appeared more like the normal controls on the MMPI profiles. Based on the familial, retrospective HK/MBD, and clinical data, it was tentatively concluded that a subgroup within the alcoholic population began drinking early in life without extrinsic precipitating causes and without manifesting obvious psychopathological disturbances. Members of this group were identified as primary alcoholics (Tarter et al. 1977) and a history of HK/MBD was postulated as an etiological risk factor. A second group of drinkers within the population of alcoholics most resembled nonpsychotic psychiatric patients; their drinking excesses began relatively later in life and did not lead to the severe consequences observed in the first group.

This latter group was classified as secondary alcoholic because members' drinking excesses were hypothesized to be responses to life crises or attempts to tranquilize themselves against psychiatric disturbances.

Having demonstrated an association between HK/MBD and subsequent adult alcoholism in a subgroup of alcoholics, four additional studies which are reported herein were conducted, to replicate the initial findings and to extend the research to other factors, including drinking patterns, psychosocial history, and psychological competence.

Experiment I: Relationship Between HK/MBD History, Psychosocial History, and Drinking Pattern in Male Alchoholics

The first study, summarized above (Tarter et al. 1977), found that primary alcoholics began drinking earlier, became addicted at a younger age, and reported more deleterious consequences from their drinking than did secondary alcoholics. A second study was designed to examine the frequency of HK/MBD characteristics in two subgroups of alcoholics, dichotomized along psychosocial criteria. Rudie and McGaughran (1961) had documented that alcoholics can be differentiated into essential and reactive types, based on maturational factors consisting of measures of social skill, drinking pattern, and age of onset, as well as other drug use. Considering that these variables differentiate alcoholics and that there is a higher incidence of familial alcoholism in the essentials (Templer et al. 1974), the two subgroups were compared on retrospective reporting of HK/MBD characteristics.

From an initial pool of 75 alcoholic subjects, 29 were classified as essential. These had a mean age and education of 37.6 years and 12.3 years, respectively; 19 were identified as reactive and had a mean age and education of 50.1 and 14.1 years. All subjects met the diagnostic criteria of Feighner et al. (1972) for alcoholism. As expected, the essentials were significantly younger than the reactives ($t = 4.65$; $p < .001$) and had a lower level of educational attainment ($t = 2.07$; $p < .05$).

The frequency of responses of the essential and reactive alcoholics on the HK/MBD checklist is summarized in table 1. The essentials endorsed a mean of 16.9 characteristics, compared with

6.8 for the reactives ($t = 5.44$; $p < .001$). These values are similar to those Tarter et al. (1977) observed between primary and secondary alcoholics, suggesting that the two classification systems may describe the same individuals. Table 1 shows that 40 of the 50 items significantly distinguished between the two groups.

The pattern of alcohol use also distinguished between the essentials and the reactives as shown in table 2. By administering the Alcohol Use Inventory (Wanberg et al. 1974), researchers found that the essentials scored higher than the reactives on general alcoholism, on an index of severity ($t = 3.83$; $p < .01$), and on all of the second-order factors. In addition, the essentials reported more drinking-related anxiety ($t = 3.72$; $p < .01$), more sustained compulsive drinking ($t = 2.15$; $p < .50$), more self-enhancement drinking ($t = 3.94$; $p < .01$), and more alcoholic deterioration ($t = 4.16$; $p < .01$).

Correlations between HK/MBD history, alcohol use, and the essential-reactive score were also quite revealing. The score on the HK/MBD checklist was highly correlated with the essential-reactive score ($r = .65$; $p < .001$), suggesting that psychosocial maturity may be strongly influenced by the presence of hyperactivity and minimal brain dysfunction characteristics. The measure of HK/MBD was also significantly correlated with several of the Alcohol Use Inventory scales such as self-enhancing drinking ($r = .60$; $p < .001$), alcoholic deterioration ($r = .61$; $p < .001$), drinking to change mood ($r = .54$; $p < .001$), and general alcoholism severity ($r = .54$; $p < .001$).

A multiple correlation was conducted on three variables, the HK/MBD score, the essential-reactive score, and the measure for general alcoholism. A score of $r = .68$; $p < .001$ was obtained, indicating that 46.8 percent of the variance of alcoholism severity could be predicted by the combined scores of retrospective HK/MBD and essential-reactive rating.

Thus, an association exists between reported childhood history of HK/MBD, severity of adult alcoholism, and psychosocial immaturity. Almost the exact number of HK/MBD features reported by the essential alcoholics in this study were endorsed by the primary alcoholics in the Experiment 1, suggesting that the two subtypes actually may constitute a single population. The primary label identifies familial and drinking variables, and the essential label describes the psychosocial and developmental correlates.

Table 1. Frequency of Endorsement by Essential and Relative Alcoholics on Childhood Questionnaire (n=19)

Characteristics	Essential Alcoholics	Reactive Alcoholics (n=19)	x^2	P<
Daydreams	79.3%	42.1%	29.01	.01
Can't tolerate delay	68.9	31.5	27.98	.01
Not working up to ability	65.5	26.3	30.94	.01
Easily frustrated	65.5	21.0	40.34	.01
Unpredictable	62.0	15.7	45.12	.01
Feeling left out	58.6	36.8	9.52	.01
Poor handwriting	55.1	42.1	3.38	ns
Lying	55.1	42.1	3.38	ns
Responds best to structured atmosphere	55.1	10.5	45.12	.01
Gets into things	51.7	36.5	4.69	.05
Difficulty in mathematics	51.7	21.0	20.37	.01
Doesn't complete projects	51.7	10.5	39.61	.01
Fidgets	48.2	21.0	16.35	.01
Short attention span	48.2	15.7	24.29	.01
Withdrawn	48.2	15.7	24.29	.01
Impulsive	44.8	36.8	1.32	ns
Demand attention and affection	44.8	21.0	12.83	.01
Wears out toys, shoes, clothes	44.8	15.7	20.07	.01
Left back in school	44.8	15.7	20.07	.01
Fights	41.3	29.3	5.03	.05
Can't sit still	41.3	15.7	16.08	.01
Can't accept correction	41.3	10.5	24.71	.01
Temper tantrums	37.9	5.2	31.62	.01
Truancy	37.9	5.2	31.62	.01
Overactive	34.4	21.0	4.48	.05
Unresponsive to discipline	34.4	10.5	16.40	.01
Unpopular with peers	34.4	5.2	26.85	.01
Steals	31.0	10.5	12.78	.01
Moves from one object to another	31.0	5.2	22.45	.01
Perseveration	27.5	5.2	18.18	.01
Vandalism	24.1	0	27.40	.01
Difficulty learning to read	20.6	10.5	3.88	.05
Talks too much and/or loudly	20.6	5.2	10.55	.01
Destructive	20.6	0	22.97	.01
Doesn't follow directions	20.6	0	22.97	.01
Rocking	17.2	10.5	1.88	ns
Infant feeding problems	17.2	5.2	7.24	.01
Accident prone	17.2	5.2	7.24	.01
Difficulty learning to write	13.7	10.5	0.48	ns
Difficulty deciding whether left or right	13.7	5.2	4.22	.05
Constantly touching other people or things	13.7	0	14.71	.01
Difficult toilet training	10.3	0	10.86	.01
Mirror vision	10.3	0	10.86	.01
Overly aggressive	10.3	0	10.86	.01
Infant sleep problems	6.8	5.2	.23	ns
Delayed time in walking	6.8	0	7.04	.01
Delayed speech development	3.4	0	3.46	ns
Poor speech	3.4	0	3.46	ns
Poor coordination	0	0	0	ns
Strabismus	0	0	0	ns

Table 2. Means and Standard Deviations of Scale Scores on the Alcohol Use Inventory by Essential and Reactive Alcoholics

	Essential Alcoholics (n=29)		Reactive Alcoholics (n=19)			
	$\bar{X}$	SD	$\bar{X}$	SD	t	P <
Social Benefit Drinking	6.97	2.13	4.00	2.49	4.407	.01
Mental Benefit Drinking	2.52	1.40	1.26	1.52	2.927	.01
Gregarious Drinking Style	5.48	2.52	4.05	1.99	2.085	.05
Obsessive-Compulsive Drinking	4.00	2.74	3.21	2.32	1.035	ns
Sustained Drinking Pattern	8.55	2.95	6.00	3.51	2.712	.01
Post-Drinking Worry, Guilt, Fear	6.79	1.95	.32	2.83	2.144	.05
Drinking to Change Mood	6.31	2.45	4.11	2.33	3.106	.01
Prior Use of External Help to Stop	3.00	2.56	2.00	2.31	1.373	ns
Loss of Control When Drinking	9.45	3.69	5.16	3.98	3.821	.01
Social Role Maladaptation	4.21	3.10	1.74	1.85	3.122	.01
Psychoperceptual Withdrawal (DTs)	4.59	3.67	1.95	1.99	2.865	.01
Psychophysical Withdrawal (Hangover)	5.90	2.38	4.05	2.32	2.650	.05
Nonalcoholic Drug Use	1.21	1.92	0.47	0.96	1.541	ns
Daily Quantity of Alcohol	4.86	2.12	4.47	1.54	.689	ns
Drinking Followed Marital Problems	1.86	1.85	0.57	0.94	2.318	.05
Drinking Provokes Marital Conflict	4.90	1.00	3.00	1.36	4.230	.01
Self-Enhancing Drinking	9.76	2.77	6.26	3.33	3.942	.01
Obsessive-Sustained Drinking	12.07	4.85	9.11	4.38	2.147	.05
Anxiety Related to Drinking	16.52	3.93	11.32	5.78	3.715	.01
Alcoholic Deterioration	18.55	7.84	10.00	5.33	4.156	.01
(Adjunct) Alcoholic Deterioration	7.69	2.44	5.63	2.75	2.718	.01
General Alcoholism	39.41	11.17	26.11	12.64	3.832	.01

Experiment II: Perceptual, Motor, and Drinking Characteristics of Primary and Secondary Alcoholics

Primary and secondary alcoholics can be differentiated on a number of variables, and the next question in Experiment 2 concerned the possibility that the groups can also be dichotomized according to certain psychological tasks sensitive to neurological integrity. Little effort has been expended to separate characteristics of hyperactivity (poor impulse control, distractibility, aggressiveness) from the "polythetic MBD syndrome" (perceptual-motor disturbance, language deficits, developmental lag, learning problems, mirror vision, mixed laterality). Hyperactivity and minimal brain dysfunction can occur clinically together or exclusive of each other. Although the terms have frequently been employed synonymously, two conditions are delineated here: (1) hyperactivity as a disturbance in activity level, impulse control, and attention; and (2) minimal brain dysfunction as a disorder of cognitive, perceptual, or motor processes. There had been virtually no research in which hyperactivity and MBD characteristics were individually assessed in alcoholics, so the characteristics measured in the checklist were presented as HK/MBD until clarification could be obtained. The study was the first attempt to delineate the HK from MBD on several performance measures.

To further delineate the characteristics of primary alcoholism, several tests were administered to measure perceptual and motor capacity. Fifteen alcoholics were each assigned to primary and secondary groups, based on the criteria previously described (Tarter et al. 1977). For unknown reasons, and unlike the previous studies, the two groups were comparable in age. The primary group retrospectively endorsed more HK/MBD characteristics ($\bar{X} = 16.0$) compared with the secondary alcoholics ($\bar{X} = 10.1$). This difference was statistically significant ($t = 2.48$; $p < .02$), even though the secondary alcoholics tended to report more features than found in previous studies.

Each group was given a questionnaire, adapted from Ludwig and Stark (1974), to assess the incidence and manifestation of their alcohol craving. In an effort to replicate Experiment 1, they were also assessed on the Rudie-McGaughran scale (1961). In addition, the subjects were given the retarded rotation test (Parsons et al. 1972), which requires the subject to rotate a knob with an attached pointer through a 180° arc as slowly as possible. To do so requires motor control and the capacity to inhibit movement. Alcoholics as a group have been found (Tarter 1976) to be deficient on this task when compared with controls, which may reflect a diminution of motor regulation or *antrieb* (Zangwill 1966). Another measure, the Stroop Test, was administered to an index of perceptual speed under normal and distracting conditions. Finally, the Gestalt Completion Test was administered; it consists of 12 fragmented pictures and the subject must construct the parts through imagery and identification of the object figure. Performance competency on this task requires spatial-synthetic or closure skills, which are frequently impaired in children suffering from MBD.

Table 3 presents the results: None of the performance measures discriminated between the two groups. Thus, the primary and secondary alcoholics are indistinguishable in perceptual speed, spatial synthesis capacity, and motor modulation.

The groups did differ on the Rudie and McGaughran essential-reactive scale ($t = 2.93$; $p < .01$), replicating the results of the previous study (Tarter et al. 1977) and demonstrating that primary alcoholism is associated with poorer psychosocial adjustment and immaturity. One other interesting finding was that the primary alcoholics described significantly more craving experiences than did the secondary subjects ($t = 3.40$; $p < .01$). The primary group endorsed a mean of 34.8 craving reactions, compared with a mean of 24.2 for the secondary subjects. The reasons for the discrepancy are unclear, but may reflect a greater generalization of external cues that elicit this emotion in the primary group, or may indicate greater physiological lability, thus rendering group members more cognizant of subtle fluctuations and states of distress, which elicit the craving for alcohol.

When the 46 items were analyzed, 12 items were found to significantly discriminate between the two groups. As shown in table 4, the primary group is more inclined to drink while under stress, when alone, and where alcohol is available. Their drinking has more tension-reducing objectives, but group members are also more likely to drink when busy, working, and successful. Thus, primary alcoholics exhibit more pervasive drinking patterns and drink when experiencing both positive and negative emotions.

In conclusion, no differences were revealed between the two alcoholic subtypes on measures of perceptual speed, perceptual organization, or motor regulation. The primary and secondary alcoholics did differ on reported childhood HK/MBD features,

Table 3. Means and Standard Deviations of Primary and Secondary Alcoholics on Craving Experience, Perception, and Motor Regulation

Measure	Group				
	Primary Alcoholics (n=15)		Secondary Alcoholics (n=15)		
	$\overline{X}$	s	$\overline{X}$	s	t
Age	41.5	8.0	44.5	10.6	ns
Rudie and McGaughran	13.6	4.2	8.6	4.9	2.93 ($p<.01$)
MBD Checklist	16.0	7.4	10.1	5.6	2.48 ($p<.02$)
Craving Checklist	34.8	5.5	24.2	10.7	3.40 ($p<.01$)
Retarded Rotation					
45^o	18.1	13.9	22.4	27.4	ns
90^o	35.8	23.1	44.5	54.2	ns
135^o	49.9	28.8	68.8	86.4	ns
180^o	62.9	33.2	89.2	110.00	ns
Stroop (time)					
Word	43.9	7.1	42.4	7.0	ns
Color	48.2	8.1	48.2	6.7	ns
Interference	60.2	12.7	59.8	12.1	ns
Word	42.1	5.4	42.1	7.1	ns
Color	46.4	10.3	45.2	6.6	ns
Interference	59.2	14.7	48.6	10.5	ns
Gestalt Completion					
Correct	5.2	2.2	5.8	2.0	ns
Time	11.6	8.1	9.1	5.3	ns

psychosocial maturity, and craving for alcohol; the latter may constitute a predisposing factor to drink. Whether that is a means of controlling inherited physiological lability, or a habit developed from learning to respond to a broad range of provoking stimuli, is, however, still unclear.

Table 4. Percentages of Subjects Who Endorsed Craving for Alcohol Items That Significantly Discriminate Between Primary and Secondary Alcoholics

Item	Primary (n=15)	Secondary (n=15)	χ^2	p<
Experience craving for alcohol when				
Under stress	93%	53%	6.13	.05
Things bad at home	93	60	4.65	.05
Alone	87	40	7.03	.01
Alcohol is available	60	20	5.00	.05
Have been successful	87	53	3.96	.05
Sober	80	27	8.57	.01
Working	67	13	8.88	.01
Busy	60	13	7.03	.01
Craving in terms of need or desire				
Get it on my mind and can't get it off	73	20	8.57	.01
Like smoking a cigarette--want it bad	80	33	6.65	.01
Craving in terms of desired effects				
Drinking takes away tension	73	27	6.53	.05
Have a drink to steady myself or get started	80	40	5.00	.05

Experiment III: Impulsivity and Personality Characteristics of Primary and Secondary Alcoholics

The previous study revealed a pattern of performance in primary alcoholics that hinted at an impairment in motor regulation, and, judging from the frequency of craving experiences, the possibility of greater physiological lability in comparison with secondary alcoholics. Experiment 3 attempted to further assess these two areas of functioning.

Twelve primary and secondary male alcoholics were identified and administered the Eysenck Personality Inventory and Kagan's Matching Familiar Figures Test. Each of the subjects in this study, as in the former ones, was tested on a voluntary basis after detoxification. In addition to the above tests, subjects were given the childhood HK/MBD checklist but, in contrast to the other studies, the two groups did not significantly differ on this measure ($t = 1.67$). Inspection of the data and reevaluation of the criteria for subject classification did not reveal any obvious reasons for this failure to replicate the previous studies. That the primary group obtained a lower mean score than formerly observed is therefore presumed to reflect random sampling factors. In any event, an interesting picture emerges when the groups are directly compared. In addition to the expected difference in length of drinking history ($t = 2.38$; $p < .05$), the primary subjects described themselves in terms indicating more neuroticism ($t = 2.19$; $p < .05$), but were not significantly different from the secondary subjects in psychoticism or extraversion on the Eysenck Personality Inventory. These findings, shown on table 5, point to greater emotional instability in the primary group. Neuroticism, according to Eysenck (1960), is conceived of as "inherited autonomic over-reactivity." A person scoring high on this measure is one with a labile nervous system; that person's consumption of alcohol may be an endeavor to reduce autonomic variability and activity.

A second finding in this study was that the primary alcoholics were as accurate as the secondary subjects on a perceptual matching task. However, the first group's response speed tended to be faster, suggesting a relative absence of detachment in analyzing the problem. The study concluded that the shorter latency indicates greater impulsivity in the primary alcoholic. This trend existed for correct responses, but was statistically significant for only incorrect

Table 5. Comparison Between Primary and Secondary Alcoholics on Drinking History, Minimal Brain Dysfunction, Personality, and Impulsivity

Measure	Group				
	Primary Alcoholics (n=12)		Secondary Alcoholics (n=12)		
	$\bar{X}$	s	$\bar{X}$	s	t
Age	37.6	11.4	42.0	15.3	ns
Years heavy drinking	12.2	7.4	6.3	4.3	2.38 ($p < .05$)
MBD checklist	13.3	7.8	8.4	6.5	1.67 ns
Eysenck Personality Inventory					
Psychoticism	2.6	2.0	2.8	2.2	ns
Neuroticism	13.3	3.8	8.8	6.0	2.19 ($p < .05$)
Extraversion	11.8	6.3	14.7	3.0	ns
Lie scale	6.8	3.2	7.8	4.0	ns
Matching figures					
# correct	5.8	3.3	6.3	1.7	ns
time (seconds)	379.8	320.7	484.6	269.5	ns
# wrong	6.2	3.3	5.8	1.7	ns
time (seconds)	230.7	128.3	449.6	205.7	3.03 ($p < .01$)

responses ($t = 3.03$; $p < .01$). On this task, impulsivity did not interfere with performance.

This study supports the hypothesis that primary alcoholics are more inclined toward impulsivity as a response style, and that they are autonomically more unstable than secondary alcoholics, as revealed by their higher neuroticism score. The neuroticism score not so extreme, however, to be of clinical diagnostic significance. Rather, the importance of this finding is the difference relative to the secondary alcoholics. Considering the wealth of psychophysiological data accrued with respect to the concomitants of neuroticism within Eysenck's schema, this difference may afford an opportunity to further examine the validity of the primary-secondary typology at a physiological level. It may also provide a heuristic and predictive picture of how each group should react to specific conditions and circumstances as well as to the effects of acute alcohol consumption.

Experiment IV: Cognitive Capacities of Primary and Secondary Alcoholics

The introduction to this paper noted that the characteristics of hyperactivity and minimal brain dysfunction often overlap. But as a polythetetic syndrome (Wender 1971), they need not coexist within the same individual. Hyperactivity characteristics were defined according to criteria pertaining to behavioral control and regulation; features of minimal brain dysfunction were identified as those processes pertaining to perceptual, cognitive, and perceptual-motor disturbances.

It is not yet determined if the etiological characteristics assumed necessary for the development of primary alcoholism reflect hyperactivity, minimal brain dysfunction, or both of these disorders. As can readily be seen, the childhood history checklist contains characteristics descriptive of both. Thus, in the tabulation of scores, the self-ratings have been tentatively described as reflecting HK/MBD characteristics. Until the two disorders can be separately evaluated in primary alcoholics, both are considered present. Thus, one research priority is to define the limits of the disorder. To this end, primary and secondary alcoholics in Experiment 2 were administered several tests sensitive to the motor control, perceptual speed, and spatial integration components of

MBD. Experiment 3 examined impulsivity, but this characteristic has frequently been reported in both MBD and hyperactivity disorders. The fourth study was conducted to determine if two alcoholic subgroups are distinguishable in terms of cognitive capacity, a dimension of functioning that is more likely to be affected by MBD than by hyperactivity.

Fifteen subjects were each assigned to the primary and secondary categories. Each subject was administered the Wisconsin Card Sorting Test, a cognitive test that measures abstracting capacity, flexibility in shifting cognitive sets, and capacity to sustain a cognitive set. This test has reliably discriminated alcoholics from nonalcoholics (Tarter et al. 1973), and test performance is related to length of drinking history. If a minimal brain dysfunction syndrome exists, certain deficits should emerge on this test—greater concept and spatial perseverative tendencies, for instance.

The results are summarized in table 6. No differences were found between the groups on any measure. The two groups exhibited almost identical cognitive capacity, and the primary subjects exhibited no tendencies for perseverative rigidity, lowered abstracting capacity, or failure to sustain a set. Thus, cognitive capacity does not distinguish primary from secondary alcoholics.

General Discussion

A research program was initiated to assess the possibility that hyperactivity or minimal brain dysfunction (Wender 1971) might serve as an etiological risk factor for one type of alcoholism. Notwithstanding the retrospective acquisition of the HK/MBD information, alcoholics, dichotomized on the basis of drinking history and style into primary and secondary types revealed consistent differences on this factor. HK/MBD may therefore be a risk factor, measurable at the behavioral and physiological levels of biological organization, may have a genetic basis in predisposing certain high risk individuals to alcoholism as well as to other psychiatric disorders (Guze 1975; Wood et al. 1976). Thus, this avenue of research affords the dual opportunity of identifying a homogeneous subgroup within the alcoholic population and of analyzing the etiological mechanisms across various levels of biological organization within this subgroup.

Table 6. Wisconsin Card Sorting Test by Performance of Primary and Secondary Alcoholics Across Set and Measures

		Set									
Variable		1	2	3	4	5	6	7	8	9	$\bar{X}$G
Trials to criterion	Primary	3.90	5.15	4.28	5.53	4.46	4.32	4.71	4.44	4.19	4.6
	Secondary	3.68	5.56	4.63	4.82	5.63	4.59	4.30	3.72	3.72	4.5
Number of errors (P + X)	Primary	1.66	2.98	1.99	3.29	2.18	1.87	2.45	2.09	1.95	2.3
	Secondary	1.54	3.10	2.54	2.56	3.08	2.25	1.96	1.47	1.52	2.2
Number of perseverative errors (P)	Primary	--	2.49	1.82	2.65	1.94	1.64	2.15	1.65	1.83	2.3
	Secondary	--	2.49	2.08	2.13	2.36	2.03	1.70	1.33	1.36	1.9
Number of other errors (X)	Primary	--	1.92	1.29	2.28	1.44	1.38	1.63	1.60	1.32	1.6
	Secondary	--	2.10	1.79	1.75	2.28	1.46	1.55	1.19	1.18	1.7
Number of perseverative errors within 10 trials of set change	Primary	--	1.95	1.68	1.78	1.75	1.39	1.57	1.69	1.61	1.7
	Secondary	--	1.73	1.71	1.57	1.49	1.55	1.37	1.23	1.37	1.3
Number of runs (≥;5 correct R's followed by error)	Primary	1.03	1.12	1.14	1.16	1.18	1.14	1.10	1.10	1.03	1.1
	Secondary	1.00	1.29	1.05	1.14	1.26	1.19	1.08	1.05	1.03	1.1

$y = \sqrt{X + 1}$ transformation for all measures except the number of runs.

Research to date has been directed toward describing the condition shared by members of this subgroup; it has been tentatively labeled primary alcoholism. The next phase will involve delineating the mechanisms involved that place a person at risk for this type of alcoholism. The five studies conducted so far support the following conclusions.

1. Utilizing specific criteria pertaining to drinking pattern and history, alcoholics can be dichotomized into primary and secondary subgroups.
2. Primary alcoholics retrospectively endorse more features suggestive of hyperactivity and/or minimal brain dysfunction than do secondary alcoholics on a childhood history checklist.
3. Primary alcoholics report a greater incidence of familial alcoholism than do secondary alcoholics.
4. There is greater psychiatric disturbance in secondary alcoholics who, on the MMPI, present a profile closer to nonalcoholic psychiatric patients. Primary alcoholics present a picture of relative normality. The latter group also exhibits less defensiveness, more energy output, and a higher score on the McAndrew Alcoholism Scale in comparison with the secondary group.
5. A childhood history of HK/MBD (that is, characteristics of psychosocial immaturity and dependency, as well as poor personal and vocational adjustment) places an individual at risk for becoming an essential alcoholic.
6. The essential alcoholic, with a high number of HK/MBD features, experiences the most deleterious drinking consequences and exhibits the most disturbed pattern of alcohol consumption.
7. The combined measures of HK/MBD and essential alcoholism can account for almost half the variance of the severity scale of the Alcohol Use Inventory.
8. Primary alcoholics report more craving experiences than do secondary alcoholics. The former group also scores significantly higher on the neuroticism scale of the Eysenck Personality Inventory, implying greater autonomic lability.

9. Psychological capacities such as motor regulation, perceptual speed, perceptual closure, and abstracting ability do not differentiate the primary and secondary alcoholics.
10. Primary alcoholics tend to be more impulsive than are secondary alcoholics.

Given these findings, a number of issues immediately present themselves.

1. The results above were obtained from retrospectively collected information. This type of study severely limits, or at least raises doubts about, the validity of the findings. Although unlikely, the primary group may present themselves in more negative terms, and thus may endorse more symptoms because of their propensity for this type of self-negation. Obviously, a prospective longitudinal study would be invaluable to confirm the findings reported here.

2. Hyperactivity and minimal brain dysfunction are controversial clinical entities insofar as diagnostic criteria are concerned. An attempt has been made to circumvent this problem in the early phase of research by operationalizing the disorder—tabulating the characteristics reported (Wender 1971) in children diagnosed as either HK or MBD. However, it is quite likely that alcoholics do not respond to all of the items with equal frequency; after a sufficiently large sample can be collected, factor analytic procedures can be applied to derive information about the items that are most discriminative and descriptive of primary alcoholism. Initial results suggest that primary alcoholics are not distinguishable on developmental maturation or perceptual-cognitive-motor disturbances. This notion is tentatively confirmed by the intact performance of primary alcoholics. Also, the frequency of endorsement of these items on the Childhood History Checklist is low. Undoubtedly, a further clarification and separation of hyperactivity-related characteristics from those associated with minimal brain dysfunction will help define the features associated with primary alcoholism.

3. Related to the issue above is the question of the content validity of the Childhood History Checklist. Does the checklist truly identify HK/MBD and, if so, is it predictive of performance? To examine this variable, the checklist was administered to 96 nonalcoholic adolescents and adults referred to the investigator for a clinical neuropsychological evaluation. It was found that the more HK/MBD features retrospectively reported, the poorer the performance on several cognitive, intellectual, and neuropsychological measures. The number of characteristics retrospectively en-

dorsed is therefore negatively related to neuropsychological competency.

The sample of 96 subjects was divided into quartiles, based on the number of HK/MBD characteristics they endorsed. The two middle quartiles were combined to yield three groups: low, medium, and high HK/MBD endorsers. The lower endorsers ($\bar{X}$ - 1.3 HK/MBD features) differed from the medium endorsers ($\bar{X} = 9.0$ HK/MBD characteristics) only on the Raven's Progressive Matrices. The low endorsers performed significantly better than the high endorsers ($\bar{X} = 25.6$ HK/MBD features) on all measures except the impairment index of the Halstead-Reitan Neuropsychological Battery. As shown in table 7, the high endorsers obtained a mean impairment index of 0.50, a value that borders on the cutoff score for a neuropsychological disorder. The medium-level endorsers performed superior to the high endorsers on five of the measures. Table 7 reveals that psychological competency progressively declines as endorsement of HK/MBD features increases. The lower end of the spectrum, where only a few items are endorsed, does not relate to performance difficulties, but the very high endorsers show significantly less competency on the various measures. The mean HK/MBD score of the alcoholics in the studies conducted so far falls in the medium or intermediate ranges, perhaps because neuropsychological deficits were not observed in the experiments. Another implication from this research is that if HK/MBD can be described, using this scale, and assuming that the scores in the adult population are normally distributed, then the secondary alcoholics would, as a group, fall below the median. The primary subjects would appear above the median, but not at a level so severe as to indicate a clinically florid HK/MBD. Thus, if HK/MBD characteristics can be assumed to constitute a normal distribution in the population and if the disorder can be quantified along a continuum of severity, then primary alcoholics are inclined toward such a disturbance, but at a subclinical level of severity. Therefore, although HK/MBD is hypothesized to be an etiological risk factor, it may not be blatantly obvious or perhaps even clinically evident in the prealcoholic.

4. The present results point to HK/MBD as an etiological risk factor for one type of alcoholism. This suggestion does not necessarily imply that such a childhood history definitely leads to alcoholism. An emerging body of evidence suggests that HK/MBD may also serve as a risk factor for other adult disorders, including sociopathy and hysteria (Guze 1975) and depression (Wood et al.

Table 7. Comparison Between Low, Medium, and High Endorsers of Characteristics on MBD Checklist on Selected Neuropsychological Measures

Measure	Low (n=24)		Medium (n=47)		High (n=25)	
	$\overline{X}$	s	$\overline{X}$	s	$\overline{X}$	s
Age	29.9	8.9	32.2	11.0	28.7	9.5
MBD checklist	1.3	1.2	9.0	3.7	25.6	6.3
WAIS						
VIQ	118.3	11.7	117.4	16.0	107.5	18.1
PIQ	113.1	13.9	109.6	14.9	102.0	15.0
FSIQ	117.0	11.3	114.6	15.3	105.2	15.9
Raven's Progressive Matrices	51.3	8.6	45.6	11.7	42.6	12.4
Wechsler Memory Scale	112.6	19.3	112.0	20.1	98.4	19.7
Impairment index	0.36	0.24	0.46	0.25	0.50	0.25
Categories (Errors)	42.5	25.6	47.2	26.3	61.1	30.7

t-tests

Low X Medium	Ravens $p < .05$
Low X High	VIQ, Categories, MQ $p < .05$ PIQ, FSIQ Ravens $p < .01$
Medium X High	VIQ, PIQ, FSIQ, Categories $p < .05$ MQ $p < .01$

1976). However, given the polythetic nature of HK/MBD, certain constellations of features may be predictive of each of these disorders. This speculation provides an alternative to the hypothesis that HK/MBD is a risk factor for all types of psychopathology. Instead, it leads to the theory that certain classes of symptoms in the HK/MBD matrix place the person at risk for one or another disorder.

Thus, although a history of HK/MBD may be a necessary condition for primary alcoholism, alone it is undoubtedly not a sufficient condition. A large percentage (perhaps one-half) of HK/MBD children and adults do not show evidence of any psychopathology (Wender 1971). Thus, a psychopathological disturbance in an individual would probably also require the presence of additional psychological problems, family and peer influences, and a learning history that determines the person's capacity and style of coping with stress.

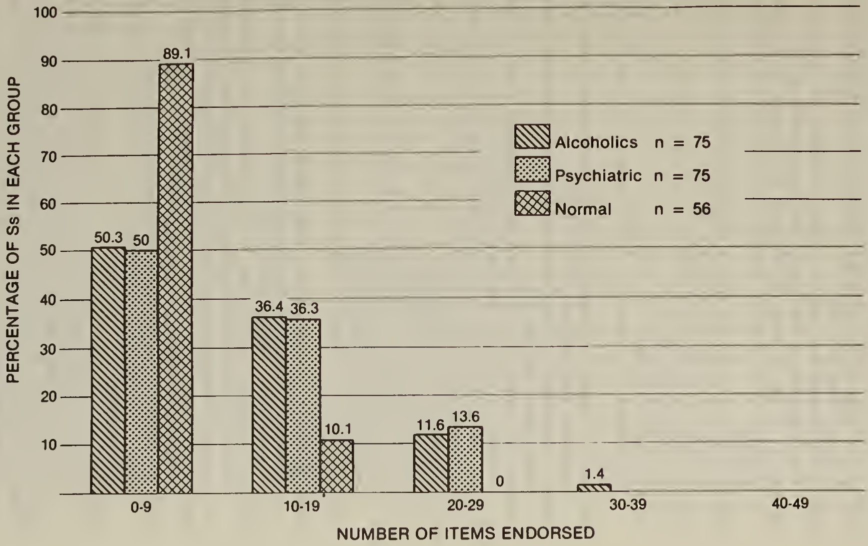
One tentative working hypothesis is that the primary alcoholic drinks to stabilize physiological lability. By smoothing out physiological reactivity, alcohol induces a subjectively perceived beneficial effect of stability and euphoria. The pleasurable state possibly also improves performance, besides being highly reinforcing. This pattern may be facilitated by the presence of environmental stimuli or interpersonal models. At least it would not be inhibited by negative sanctions. These personal results lead to an almost immediate pattern of excessive consumption. Consequently, addiction ensues relatively quickly, and whatever short-term benefits accrue from the acute effects of the ethanol are more than offset by the deleterious effects of the addiction. Not surpisingly, primary alcoholics report a positive euphoric response in their first drinking experience, drink for the desired effect, and are less likely to drink because of a precipitating stress. Alcohol is therefore a prime drug of choice for such individuals. In addition to its well-known depressant effects, alcohol also has central stimulatory qualities through the metabolite acetaldehyde (Truitt and Walsh 1971). The effects of acetaldehyde closely resemble those produced by d-amphetamine, and it is therefore quite possible that the hyperactive disturbance predisposes the person to self-selection of alcohol for its stimulating qualities.

Thus, a theory of primary alcoholism is tentatively offered: HK/MBD is hypothesized to be a behavioral risk factor for adult alcoholism, although other factors are undoubtedly involved as well. What is somewhat loosely described as HK/MBD may eventually be more parsimoniously understood at the biochemical and physiological levels. However, the present hypothesis provides a heuristic framework in which to develop a unifying classification system of alcoholism; biological and psychological data can be integrated to develop a comprehensive clinical picture.

What needs to be reiterated is the observation that HK/MBD is not specific to alcoholism. Why some individuals become alcoholic and others do not is, of course, a pressing issue. HK/MBD may be a risk factor for psychopathology generally, or different clusters of symptoms in this polythetic syndrome may place a person at risk for one specific type of disorder or another. In any event, as figure 1 shows, administering the Childhood History Checklist to groups of unselected male alcoholics, neurotic psychiatric patients, and normals, produces almost identical results from the alcoholics and the psychiatric patients. Some 90 percent of the normals endorse 9 characteristics or fewer, 50 percent of the alcoholics endorse 10 or more. None of the normals endorsed more than 20 HK/MBD characteristics, but approximately 12 percent of the alcoholics and 14 percent of the psychiatric patients endorsed that many. Thus, the normals are skewed toward the low end of the distribution, and the alcoholics and psychiatric patients are overrepresented at the higher end. Even though these findings are based on a small sample size, these data provide challenging confirmation that HK/MBD may be an important variable.

Future research should strive to clarify, in more precise terms, the homogeneous typology of primary alcoholism. Then it would be possible to elucidate the neurochemical and physiological mechanisms that are behaviorally described here as HK/MBD. Investigators could develop primary and secondary prevention techniques; the prealcoholic or early stage alcohol abuser could be identified before personal and social deterioration occur. Thus, the study of etiological mechanisms is crucial. The notion of HK/MBD is but one heuristic approach toward understanding one type of alcoholism.

Figure 1. Distribution of Alcoholics, Psychiatric Patients, and Controls, According to Number of Characteristics Endorsed on Childhood History HK/MBD Checklist



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DISCUSSION OF PAPERS BY GOODWIN, HESSELBROCK, REICH, AND TARTER

James R. Stabenau

These four papers present data on genetic, central nervous, and sociocultural vulnerability, all crucial issues in understanding the pathogenesis and transmission of alcoholism.

Dr. Goodwin reviewed attempts to assess the relationship between the ubiquitous use of alcohol and the distribution of alcohol addiction in families, including a synopsis of pedigree, twin, and his own Danish adoptee studies of alcoholism. Pedigree studies say only that alcoholism is a family-related disorder and that males are more clearly affected than females. Additional data has emerged from the twin studies, suggesting a genetic hypothesis, but similarities of family environment have not been controlled for. Goodwin also explains the adoptee study design, which controls for differences in genetic heritage and environmental influences. From these data, it is clear that individuals with a biologic heritage of parental alcoholism have an equal risk of becoming alcoholic in adulthood, whether reared by nonalcoholic adoptee parents or by their own alcoholic parents. Goodwin notes that females adopted out do not have a significant appearance of alcoholism in the adoptee studies. But he also points out that 90 percent of the women were abstainers or drink minimally, and 40 percent of the male adoptees were heavy drinkers. This grouping of data then suggests that there is a significant genetic vulnerability for alcoholism, and that predisposed individuals, given sufficient exposure to alcohol in quantity and duration, whether male or female, will develop alcoholism. This is not unlike the environment heredity formulation made for schizophrenia (Stabenau 1968).

Alcoholism is currently considered a heterogenous typology, including at least four dimensions: (1) genetic predisposition; (2) psychosocial history; (3) alcohol consumption patterns; and (4) personality traits.

Dr. Hesselbrock, in her study of 24 female and 30 male alcoholics, reaffirms previous observations about differences in life experiences of female and male alcoholics. For example, female alcoholics were less deviant in childhood, more often had an alcoholic parent, and are more likely to have had multiple psychiatric problems leading to treatment. Important new data are presented dealing with the differences in stages of alcohol use by females.

The profile of alcohol addiction in Dr. Hesselbrock's study appears to show that women progress more slowly than men from the first drink to regular intoxication; after women begin to get drunk regularly, they seem to progress to problem drinking much faster than do men; and women seem to accept that they are alcoholics and seek treatment more quickly than do men.

Dr. Hesselbrock's data confirm Goodwin's suggestions that sociocultural factors may explain these differences. But one observation may shed some light on different mechanisms leading to the use of addicting quantities of alcohol: "Women begin regular drinking after realizing alcohol gives relief."

These data, if replicated in the larger sample, suggest that women do have a genetic vulnerability to alcoholism equal to that of men. But because women tend to begin regular drinking later than men, they do not as a group drink sufficient quantities of alcohol to precipitate alcohol addiction in as many instances.

Dr. Reich and his colleagues provide data on alcoholism in families of alcoholics and antisocial personality disorder in a study of 74 proband and 89 control families (Reich et al. 1975). Diagnosis was obtained by interviews, with probands, their spouses, and first-degree family members. The researchers applied multifactorial correlational equations to the data, and significant new findings emerged from imaginative hypothesis testing.

1. Severity of drinking does not appear to be transmissible.

2. Antisocial personality appears to be genetically separate from alcoholism, but interacts with alcoholism to produce even higher incidence in first-degree family members.

3. Lower frequency of alcoholism in females is environmentally determined by their lower frequency, quantity, and duration of alcohol use.

Reich also noted that families broken by divorce appear not only in proband families but in families of origin too, and that a significant number of dual alcoholic matings occurs, suggesting that assortative mating should be considered in future models of the transmission of alcoholism.

Tarter added a neurophysiologic typology dimension in an attempt to relate childhood MBD and the hyperkinetic syndrome to the development of alcoholism in adulthood. His hypothesis is that hyperactive behavior in childhood, as exemplified by restlessness, impulsivity, destructibility, lability, and aggressiveness, reflects a genetically determined neurophysiologic "disturbance in modulating arousal mechanisms." He postulates that the primary alcoholic, who begins drinking early in life, becomes addicted without extrinsic precipitating cause, suffers more alcoholic deterioration, and exhibits little obvious psychopathology, has significant history of hyperkinetic and/or minimal brain damage symptoms in childhood.

Dr. Tarter developed a classification of primary and secondary alcoholism from a dichotomization of alcoholics by number and variety of childhood HK and MBD symptoms. The new study tests the hypothesis in new samples. In one sample of alcoholics, Tarter found that 60 percent of 48 alcoholics were classed as "essential," according to Rudie and McGaughran criteria. This sample, with its higher incidence of familial alcoholism and maturational immaturity, was considered synonymous with the primary alcoholic classification. Reactive alcoholics were considered secondary alcoholics.

Tarter postulates that "psychosocial maturity may be strongly influenced by the presence of hyperactivity and minimal brain damage characteristics." He attempted to ascertain if differences in neurological integrity as determined by psychological tasks, can distinguish primary from secondary disorders. In a new subsample of 15 primary and 15 secondary alcoholics, he found no differences in "perceptual speed, spatial synthesis capacity, and motor modulation." A third and different sample of 12 primary and 12 secondary alcoholics was tested for neuroticism. These two groups did not differ on the HK/MBD checklist scores. Tarter did find these primary alcoholics to have shorter latency on a matching test. He concluded that these data "indicate greater impulsivity in the primary alcoholic." The sample was not high on HK/MBD criteria. I question the conclusion from this small sample that "they (primary alcoholics) are autonomically more unstable."

Assuming that either or both HK and MBD are etiological in some alcoholics, Tarter then attempts to distinguish HK from MBD by means of cognitive tasks. Another set of 15 primary and 15 secondary alcoholics was studied, but no differences were found in cognitive capacities.

Tarter concludes from these samples that "the primary alcoholics are not distinguishable on developmental maturation or perceptual-cognitive-motoric disturbances." Thus, these studies do not directly advance the theory that childhood MBD or HK can be detected in adult alcoholics. Nor can such history be specifically related to primary or essential alcoholism, because HK and MBD checklist items are not specific for alcoholics, but are associated with a range of adult psychopathology.

Any further research in this area might approach primary and secondary alcoholism as a spectrum disorder ranging from patients with normal scores to patients with a history of HK and MBD; and from heavy drinking to the alcohol-addictive state. Outcome studies of hyperkinetic and MBD children as adults are necessary to assess scientifically any relation to adult clinical alcoholism.

Each of these papers presents new data on addictive alcoholism, and attempts to fit the observations into a model of transmission of alcoholism in men and women.

Goodwin's review of the family and alcoholism suggests that individuals with alcoholism in their biological parents have an equal risk of becoming alcoholics in adulthood, whether raised by nonalcoholic adoptee parents or by their own alcoholic parents. Tarter's characterization of some alcoholics as "primary" turns research attention to what may be inherited as a biological predisposition to alcohol addiction, and what congenital or developmental-environmental experiences may interact with the genetic to lead to a vulnerability to alcoholism. Hesselbrock's study moves from the issue of biological-environmental factors to sociocultural factors that might be of equal importance to understanding why the vulnerable female becomes or does not become alcoholic.

Reich's gene-environment interaction model provides the framework for testing the relative importance and interaction of the genetic, environmental, and sociocultural factors in the transmission of alcoholism.

Reich and his associates have provided a research model for analyzing the contribution of genetic and environmental factors in the transmission of psychiatric disorders, including alcoholism (5). The multifactorial model of disease transmission emerges out of quantitative genetics. Psychiatric disorders such as alcoholism have been considered as semicontinuous variables—that is, those affected can be detected because they exhibit a degree of that condition, but unaffected people cannot be so identified. This model is a device for quantifying family data, discriminating between different modes of transmission, and studying variations in disorders according to variables such as age, sex, and severity of illness (5).

Reich provided a sophisticated means of mathematically assessing the use of such a model to analyze the contribution of genes and environment in alcoholism. Mathematical models used in genetics usually assume that the effect of any single gene is small. But for polygenically transmitted traits, these effects are equal and additive. If the inheritance of alcoholism is multifactorial, then it is seen clinically only when the critical contribution of genetic and environmental factors increases the individual's risk or his liability for alcoholism beyond a definite threshold, that is, to the state of alcohol-addictive symptomatology. Only those individuals with a liability that exceeds that threshold will show clinical alcoholism. Models such as these are helpful in making approximations, but are based on assumptions that do not always apply in the condition or sample studied. But these models do allow for a more moderate view of factors that are part of what we colloquially refer to as "heritability." For example, correlation of a trait like alcoholism among family members is due to at least three different factors: (1) the additive genetic contribution due to shared genes; (2) the nontransmissible contribution to alcoholism from the sharing of a common family, the sociocultural environment; and (3) the transmittal between relatives, the human social interaction cultural factor. Each of these factors interacts with the others. As Reich illustrates, when the importance of any of these genetic or environmental factors is determined (usually by correlation between the factor and the appearance of alcoholism), it is possible to analyze the interplay of these factors within the framework of equations. The extensions of a multifactorial analysis can be very complex. But with suitable application, it may be possible to derive good estimates of the parameters required for alcoholism to appear in the individual and regarding the distribution of alcoholism in the family.

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SESSION IV: BEHAVIORAL ASSESSMENT OF THE ALCOHOLIC

LOSS OF CONTROL AND THE PROBLEM OF CRAVING

Arnold M. Ludwig

It is interesting that "authenticity" of the phenomena of craving and loss of control, the traditional descriptive cornerstones for alcoholic behavior, should be a subject of scientific dispute and controversy. Unfortunately, much of this controversy is more ideological than real in nature, contraposing a restrictive medical-disease model against a social-learning, behavioral one. The "strawman" for the restrictive medical-disease model, which emphasizes genetic predisposition, the operation of neurophysiological mechanisms, and the pharmacological properties of alcohol itself, is the relative unimportance of environment in accounting for alcohol addiction and its physical complications. The "strawman" for the behavioral model, which emphasizes environmental contingencies controlling alcoholic behavior, is the relative unimportance of intrinsic motivational states or biological factors in accounting for the behavior of alcoholics in laboratory or experimental settings. The problem with both viewpoints is they are at the same time both right and wrong; they are right in their emphasis and wrong in their deemphasis. In my opinion, any integrative, explanatory theory of alcoholic behavior must accept certain fundamental principles relating to all human behavior.

1. Human beings experience motivations and drives, either innate or acquired (hunger, sex, curiosity), which may or may not be expressed in behavior.

2. Human beings engage in mentation and decisionmaking (even though these processes cannot be directly observed or measured), which may or may not be expressed in behavior.

3. The brain is the organ of behavior. As such, it requires a physiological support system for optimal functioning. Disruptions in brain function will have profound effects on expressed behavior.
4. Behavior must occur within an environmental context. Environmental stimuli or contingencies, in turn, may have profound effects on shaping behavior.

Surprisingly, these simplistic truisms seem to have been relatively ignored in the scientific study and theory construction of alcoholism and, most certainly, in its comprehensive treatment. Disease-oriented approaches have not adequately accounted for the environmental and situational factors that affect drinking behavior or of the ability of these factors to become conditioned stimuli for alcohol acquisition and consumption. Behavior-oriented approaches have not adequately accounted for the physiological status of the individual, especially during hyperarousal, or for the potential cognitive deficits that predispose an alcoholic to drink.

This paper does not speculate on how alcoholics become alcoholics; this has been done elsewhere (Ludwig in press). These comments mainly concern the end-stage drinking behavior of those individuals who have become physically dependent on ethanol—people who have experienced episodes of withdrawal symptomatology in response to abrupt drops in blood alcohol level. In these particular individuals, certain phenomena governing drinking behavior are far more prominent than in other types of problem drinkers, such as binge or situational drinkers, whose physical dependence is not advanced beyond hangovers and mild tremor. Similar factors operate in binge and situational drinkers as in physically dependent alcoholics, but the determinants of drinking are often overshadowed by more motivational and situational factors.

The major question for discussion here is why alcoholics drink, and, once drinking, why they continue to drink far more and for a longer time period? This question leads directly to the issues of "craving" and "loss of control." For definitional purposes, craving represents the cognitive state designating ethanol consumption as a source of relief or pleasure. It need not inevitably lead to drinking. Loss of control is the behavioral state initiated by craving and characterized by activities indicative of a relative inability to modulate ethanol consumption. It need not always result in gross intoxication or stupor (Ludwig and Wikler 1974).

Craving for alcohol is comparable to narcotic "hunger," in that craving represents the psychological or cognitive correlate of a "subclinical" conditioned withdrawal syndrome. Along with the development of physical dependence on alcohol, alcohol withdrawal phenomena can become classically conditioned to certain stimuli (physical environment, bar setting, sights and smells associated with alcohol consumption, certain emotional states) through repeated temporal associations between these stimuli and "unconditioned" alcohol withdrawal phenomena. Alcohol acquisition behavior is repeatedly reinforced (instrumental conditioning) by the success of alcohol consumption in suppressing withdrawal symptomatology. Also, the anxiety due to withdrawal and its consequent relief by alcohol help to establish a pattern of relieving anxiety due to other factors. Therefore, after conventional detoxification and discharge of patients to their home environments, exposure to the same or similar stimuli can now evoke conditioned withdrawal phenomena and alcohol acquisition behavior or relapse.

Craving provides the alcoholic with the necessary cognitive symbolism for goal-directed, appetitive behavior, and there is no cogent reason why this subjective desire for alcohol should be directly acted on or expressed in overt behavior, especially if there are competing drives or motivations. Craving, then, can be regarded as a necessary but not sufficient condition for relapse or loss of control.

Craving can be evoked through interoceptive or exteroceptive stimuli. Interoceptively, craving can be elicited in alcoholics through administration of low doses of tetrahydrocannabinol (THC) (Ludwig 1975), the effects of which resemble those of alcohol, or even the administration of lysergic acid diethylamide (LSD), the effects of which may produce a "hangover" or delirium tremens (Ludwig et al. 1969). Subjective reports of craving are most commonly associated with dysphoric states, such as depression or nervousness (Ludwig and Stark 1974) or somatic symptomatology (Hore 1972), which are not so different from what alcoholics experience during withdrawal. Exteroceptively, craving for alcohol can be easily evoked through exposure to familiar environmental cues conducive to drinking (Ludwig et al. 1974; Ludwig, Cain, Wikler, Taylor, and Bendfeldt 1977).

The most powerful evocation of craving and consequent alcohol acquisition behavior occurs through the combination of appropriate interoceptive and exteroceptive stimulation (Ludwig et al. 1974). In a conducive drinking setting such as a bar atmosphere, consumption of a small to moderate amount of alcohol contained in the alcoholic's favorite mixer yields far more craving and alcohol acquisition behavior than administration of placebo or high initial doses of alcohol. Consumption of any of these agents under conducive conditions tends to induce more craving and alcohol acquisition than consumption under nonconducive conditions such as in a research laboratory. These findings are important in two respects. First, they attest to the importance of both pharmacological and environmental cues in the production of craving and alcohol consumption. Second, they offer a potential basis for explaining discrepant research findings about these phenomena. Craving and inordinate alcohol acquisition are not prominent when studies are conducted in sterile, institutional, nonconducive drinking settings.

In essence, these studies support the Alcoholics Anonymous caveat about the danger of the "first drink." In our studies (Ludwig et al. 1974), the equivalent of one to two cocktails, administered under conducive drinking conditions, seems to act as an hors d'oeuvre, stimulating or whetting appetite for more alcohol. This initial drink appears chain-conditioned to the consumption of sufficient alcohol to reach what we have termed the alcoholic's pharmacological ceiling.

Craving and alcohol acquisition do not always have a "one-to-one" relationship. A high intercorrelation is far more likely under conducive than nonconducive drinking situations (Ludwig et al. 1974). Certain physiological states aside from craving may also predispose a drinker to alcohol acquisition and consumption. In one study (Ludwig, Cain, Wikler, Taylor, and Bendfeldt, 1977), most of the total variation of work-for-alcohol measures could be accounted for on the basis of increased craving, alpha activity, diastolic blood pressure, respiratory rate, and decreased blood pressure. In another study (Ludwig, Cain, and Wikler 1977), alcoholics were classified on the basis of whether they chose to work for and consume alcohol. About 77 percent could be correctly classified by discriminant function analysis on the basis of craving, subjective arousal, and cortical average evoked response type. With this latter measure, "augmentation" appeared to be a necessary but not sufficient condition for those who chose to work for and consume alcohol.

The phenomenon of loss of control is complementary to that of craving. At the outset, it is necessary to emphasize that this phenomenon has engendered considerable misunderstanding. Alcoholics who report or display loss of control need not, as servomechanisms, always drink to the point of gross intoxication or stupor. This phenomenon is a relative one, simply indicating that alcoholics tend to lack the capacity, over time, to regulate or modulate their ethanol intake short of intoxication. After the first drink or two, excessive alcohol consumption may occur immediately or build up over a span of weeks or months. For Keller (1972), the hallmark of loss of control is the inability to refrain from relapse.

While chain-conditioning may account for much of the alcoholic's relative inability to regulate ethanol intake according to personal or medically indicated limits, other factors also may complicate this situation, thereby making the prospects of social drinking unfeasible. Some obese individuals appear to suffer from an interoceptive cue dysfunction, wherein subjective reports of hunger do not correlate with hunger contractions of the stomach and food satiety is poorly perceived. Alcoholics may have a comparable type of neurophysiological feedback dysfunction. In contrast to social drinkers, who can easily be taught to discriminate their blood alcohol levels accurately (Huber et al. 1976), chronic alcoholics seem to display much more difficulty (Silverstein et al. 1974). In this author's studies (Ludwig et al. 1978; Ludwig, Bendfeldt, Wikler, and Cain 1977) research subjects were exposed to a long training session dealing with the identification of internal cues associated with a stable blood alcohol level. Fifty percent of the alcoholics, and only 5 percent of the social drinkers, displayed drinking behavior indicative of loss of control over keeping their blood alcohol levels within a specified, socially desirable range. At a series of drinking decision points, alcoholics display significantly more errors of commission than do social drinkers. The drinking patterns of subjects could be manipulated somewhat by the nature of the feedback provided to them. These studies did not determine whether the presumed cognitive deficits underlying this feedback dysfunction result secondarily from prolonged alcohol use (thereby aggravating the situation) or existed before the development of physical dependence (thereby facilitating this process).

In conclusion, these studies simply confirmed what most clinicians, alcoholics, and members of Alcoholics Anonymous have long known—craving and loss of control are "real" phenomena and play a crucial role in the understanding of alcoholism. Individual psychological, situational, and environmental factors may also substantially influence the expression of these phenomena, but theoreticians or researchers who discount the existence of craving and loss of control have abandoned the very essence of alcoholism. Most likely, experimental studies that failed to confirm the operation of these phenomena in addictive drinking behavior (a) have been confined to heavy, binge, or situational drinkers, who showed little evidence of prior physical dependence; (b) have evaluated subjects under nonconducive, artificial drinking conditions; or (c) did not ask alcoholics why they drink, or applied highly restrictive criteria for evaluating loss of control. Of even greater import, what scientific information is known about these phenomena has barely been used to develop comprehensive treatment programs for alcoholics.

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THE ROLE OF AVERSIVE CONSEQUENCES IN THE CONTROL OF ALCOHOL AND DRUG SELF-ADMINISTRATION*

Nancy K. Mello

Introduction and Overview

This essay examines some commonly held beliefs and clinical data about the behavioral effects of alcohol and discusses their implications for understanding the factors that maintain alcohol abuse. There is accumulating evidence that alcohol may have some aversive consequences during intoxication as well as the expected positive effects. These aversive consequences of drinking indicate that the behavioral effects of alcohol are more complex than concepts related to hedonism would suggest. Recent clinical and experimental evidence that aversive or noxious events can control behavior leading to their repetition as effectively as positive events will be reviewed.

These issues are considered within the broader context of factors that maintain other forms of substance abuse. Traditionally, alcoholism and problem drinking have been studied in isolation from other drug abuse problems. The tendency to focus on specific syndromes associated with the abuse of particular drugs such as alcohol, heroin, and cocaine has militated against appreciation of possible similarities between drugs. Moreover, known differences in the pharmacological and behavioral consequences of alcohol, heroin, and cocaine intoxication seem to argue against the notion that any meaningful similarities could be found.

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* Preparation of this paper was supported in part by grants DA 70676 and DA 02519 from the National Institute on Drug Abuse, and grant AA 04368 from the National Institute on Alcohol Abuse and Alcoholism. This paper was adapted from "Control of Drug Self-Administration: The Role of Aversive Consequences," by N. K. Mello, which appeared in *Phencyclidine (PCP) Abuse: An Appraisal*, R. C. Petersen and R. C. Stillman, eds. NIDA Research Monograph Series, No. 21, DHEW Publ. No. (ADM)78-728, 1978, pp. 289-308.

In opposition to the usual separatist approach to alcohol and drug problems, it will be argued that a *comparative* study of drug abuse problems may prove to be very important for clarifying the bases of these complex addictive behavioral disorders. The emergence of the term *substance abuse* into common parlance may facilitate the comparative study of alcohol and drug problems (Mello 1980). The potential importance of attempting to identify commonalities across various forms of substance abuse is increasingly recognized (Committee on Substance Abuse and Habitual Behavior 1977). Documentation of the prevalence of polydrug problems involving alcohol (Bourne 1975; Maddux and Elliott 1975; Schut et al. 1973) further argues for attention to the similarities as well as the differences between various types of substance abuse.

Many drugs of abuse have now been shown to have aversive consequences during intoxication. These data have led to the hypothesis that "aversive" consequences may be an important factor in the control of many forms of drug abuse (Mello 1977, 1978). Findings relevant to this hypothesis will be examined in the remainder of this review. One basic assumption is that drug self-administration behavior is controlled or maintained by its consequences. Therefore, any consequence that occurs consistently and transcends drug-specific effects may be a common factor that contributes to the maintenance of substance abuse.

Behavioral Effects of Alcohol and Opiates

It is generally acknowledged that the long-term effects of chronic substance abuse are adverse and may compromise employability as well as disrupt family and social relationships. However, the immediate consequences of drug use are usually believed to be sufficiently positive to outweigh these long-term effects. If, in fact, abused drugs consistently produced relaxation, euphoria, relief from anxiety, tranquility, and serenity, then chronic drug use and abuse might be more understandable. However, common expectancies about drug-related pleasures have not been confirmed in clinical studies of addicts during intoxication. Direct observations of intoxicated individuals are often discordant with retrospective self-reports of drug effects obtained during a period of sobriety. This discrepancy is particularly troublesome since most of our information about the effects of abused drugs is based on retrospective reports of users during sobriety. However, evidence from inpatient clinical studies now indicates that increases in dysphoria, anxiety, and agitation frequently accompany chronic alcohol intoxication (Mello and Mendelson 1978) and heroin intoxication (Mirin et al. 1976; Meyer and Mirin 1979).

Behavioral Effects of Alcohol Intoxication

Traditionally alcohol has been considered a euphoriant, and a variety of positive effects including anxiety reduction, alleviation of depression, and facilitation of social interaction are ascribed to alcohol intoxication. Although retrospective reports of a drinking experience obtained from alcoholics during sobriety usually attest to the pleasures of drinking, direct observation of alcoholics during intoxication have shown that the opposite is usually true. A list of some of the subjective states that alcohol is believed to improve or enhance, and empirical findings from clinical studies of intoxicated individuals, are summarized in figure 1 (cf. Mello and Mendelson 1978 for review). Curiously, the alcoholic appears not to recall the aversive aspects of intoxication during a subsequent period of sobriety, but rather reports his expectancies about the positive effects of alcohol (McGuire et al. 1966).

Dysphoria and anxiety associated with alcohol intoxication are not restricted to the alcoholic, but may also occur in social drinkers. The major determinant of the behavioral effect of alcohol appears to be the dose of alcohol consumed, relative to the experience and behavioral tolerance of the drinker. Low doses of alcohol, sufficient to produce a blood alcohol level of between 30 and 50 mg/100 ml often produce the anticipated pleasurable consequences (cf. figure 1). However, social drinkers report increased depression, dysphoria, and anxiety after an acute high dose of alcohol of 6 to 8 ounces (Williams 1966; Warren and Raynes 1972). Alcohol addicts often ingest between 26 and 32 ounces of distilled spirits per day (or the equivalent in beer or wine) (Mello and Mendelson 1978).

Figure 1. Schematic Summary of Clinical Studies of the Behavioral Effects of Alcohol

OBSERVED EFFECTS OF ALCOHOL

	LOW DOSE	HIGH DOSE
MOOD	↑	↓
ANXIETY	↓	↑
DEPRESSION	↓	↑
SOCIABILITY	↑	↓
AGGRESSION	↑	↑
SEXUALITY	↑↓	↑↓
RELAXATION	↑	↓
SELF–IMAGE	↑	↓
FANTASY–REVERIE	↑	↑
SLEEP	↓	↓

Adapted from Mello, and Mendelson, 1978. Elevation or enhancement are indicated by ↑; Depression or impairment by ↓.

Since alcohol-tolerant addicts have a greater tolerance for alcohol, larger amounts are required to produce increased depression and anxiety than for the social drinker. Clinical studies from many laboratories, employing a variety of techniques, agree that chronic intoxication, sufficient to maintain blood alcohol levels between 150 and 300 mg/100 ml, is associated with increased depression, agitation, anxiety, and belligerence in the drinker (Mello and Mendelson 1978). Severe chronic alcohol intoxication may also be associated with illusions and hallucinatory experiences during drinking as well as during alcohol withdrawal (Wolin and Mello 1973).

Behavioral Effects of Heroin Intoxication

Retrospective reports of the effects of heroin intoxication by heroin addicts emphasize euphoria and serenity. As Jaffe (1975) described it,

> Narcotics do more than produce indifference to pain. They also suppress those drives that motivate an individual to appease hunger, seek sexual gratification and respond to provocation with anger. In short, they seem to produce a state of total drive satiation. Nothing needs to be done because all things are as they should be. For certain types of personalities, but clearly not for all, such a state is extremely pleasant. (p. 284)

Clinical observations of heroin addicts during a period of opiate intoxication are at variance with this impression. Chronic opiate use is often accompanied by an increase in dysphoria, irritability, hypochondriasis, psychopathology, belligerence, negativism, and motor retardation (Wikler 1952; Haertzen and Hooks 1969; Mirin et al. 1976; Meyer and Mirin 1979). The dysphoric consequences of chronic heroin intoxication appear to be directly related to heroin use rather than to situational or social factors. Heroin addicts, maintained on the long-acting opiate antagonist naltrexone during the same period of residence on a clinical research ward, did not develop dysphoria, anxiety, or belligerence comparable to that shown by heroin users (Mirin et al. 1976; Meyer and Mirin 1979). It could be argued that a brief and transient positive mood change, which is purportedly associated with the induction of alcohol and heroin intoxication, is sufficient to maintain drug self-administration behavior (Mirin et al. 1976; Davis 1971). In the case of heroin addiction, the intensity of the positive feelings associated with the rush appear to be attenuated as tolerance develops during the course of chronic heroin use (Meyer and Mirin 1979).

Effects of Drugs in Naive Users

In thinking about the way in which drugs come to control behavior leading to their self-administration, it is instructive to review some reported effects of acute drug use by naive users. It would be convenient if the initial drug experience was so overwhelmingly positive that repeated drug use would be almost inevitable. Yet the reported effects of acute doses of opiates, barbiturates, alcohol, and nicotine summarized in table 1 do not appear to be especially appealing. These drugs each produce a variety of somatic and emotional effects that would seem disadvantageous to the user. Yet, despite these "aversive" consequences of initial drug use, many individuals persist in self-administration of these same drugs to the point of abuse and addiction.

It has often been observed that alcohol addicts tend to have a clear recollection of their "first drink" (Kuehnle et al. 1974). However, clinical impressions suggest that the first drink was not memorable because of its relaxing, euphorigenic, tension-reducing, and self-actualizing effects for the drinker (Kuehnle et al. 1974; Catanzaro 1968). It is more likely that the future alcoholic drank to the point of intoxication with associated despondency, nausea, and vomiting.

The process by which an initial aversive drug experience becomes translated into a repetitive drug use pattern is not understood. It could be postulated that with the development of drug tolerance, these seemingly unpleasant somatic and emotional effects undergo a transition to a more positive state, such as euphoria, relaxation, and tranquility. Alternatively, it could be postulated that the initial adverse reactions—dysphoria, nausea, and vomiting—are an integral part of the reinforcing properties of subsequent drug abuse. It is evident that drug abuse is maintained despite the recurrence of these seemingly aversive consequences. The repetitive use of phencyclidine is an extreme illustration of this phenomenon. Its acute effects include dose-related illusions, dissociation, perceptual disturbances, often associated with agitation and violent behavior, which may culminate in convulsions, coma, and catatonic immobility. It would be difficult to categorize these as "positive" effects, yet there was a 50-percent increase in users in the 18- to 25-year-old group between 1976 and 1977. Phencyclidine self-administered by 12- to 17-year-old youth also increased from 9.5 to 13.9 percent during this period (Stillman et al. 1980; Petersen and Stillman 1978). The development of a toxic psychosis does not seem to be a serious deterrent to repeated phencyclidine use. Comparison with the consequences of alcohol and heroin intoxication suggests that phencyclidine abuse differs primarily in the intensity of its aversive effects.

Animal Models of Aversive Stimulus Self-Administration

Although it is tempting to dismiss clinical data on the aversive effects of drug use as optimistic expectancies failed, the quest for aversive stimulation is not restricted to man. There is evidence that seemingly aversive consequences will also maintain self-administration behavior in animals under certain conditions. Two examples of aversive stimulus self-administration are narcotic antagonist self-administration and electric shock self-administration.

Narcotic Antagonist Self-Administration

Narcotic antagonists induce withdrawal signs in opiate-dependent monkeys. A summary of some typical withdrawal signs appears in table 2. It is evident that the somatic consequences of opiate withdrawal resemble some consequences of acute intoxication in naive drug users shown in table 1. It is not surprising that opiate-dependent monkeys will work to escape and to avoid the infusion of narcotic antagonists (Downs and Woods 1975; Hoffmeister and Wuttke 1973). However, it has also been found that under certain conditions morphine-dependent monkeys will work to produce injections of narcotic antagonists.

Goldberg and coworkers (1972) were the first to observe self-administration of the narcotic antagonist nalorphine by opiate-dependent monkeys. During studies in which either saline or nalorphine was substituted for morphine injections during a 7.5-hour session it was found that responding that was followed by nalorphine injections was maintained at a higher rate than

Table 1. Some Reported Acute Effects of Drugs in Naive Users*

	Opiates	Barbiturates	Alcohol	Nicotine
Nausea	X		X	X
Vomiting	X		X	X
Dizziness	X			X
Sweating				X
Dysphoria	X	X	X	
Emotional Lability		X	X	
Aggressivity			X	
Impairments In				
Concentration	X	X	X	
Thinking	X	X	X	
Comprehension		X	X	
Memory		X	X	
Judgment		X	X	
Drowsiness	X	X	X	
Lethargy	X	X	X	

*Adapted from Jaffe 1975, Mello and Mendelson 1976; Russell 1976.

responding that was followed by saline injections. The distribution of responses within successive 2.5-hour segments of the 7.5-hour saline and nalorphine substitution sessions is shown in figure 2. It is apparent that nalorphine maintained responding. Monkeys continued to self-administer nalorphine despite severe withdrawal signs which included vomiting, coughing, salivation, tremors, and irritability. Responding for nalorphine did not extinguish during the substitution sessions.

These data indicate that, under certain conditions, response-produced nalorphine injections can maintain responding in monkeys which are physiologically dependent upon morphine. Goldberg and coworkers concluded that these findings illustrate that the experimental history of the organism, and the behavioral schedule under which a stimulus event is presented, rather than the type of event, may determine the effect that an event may have upon behavior (Goldberg, Hoffmeister, and Schlichting 1972).

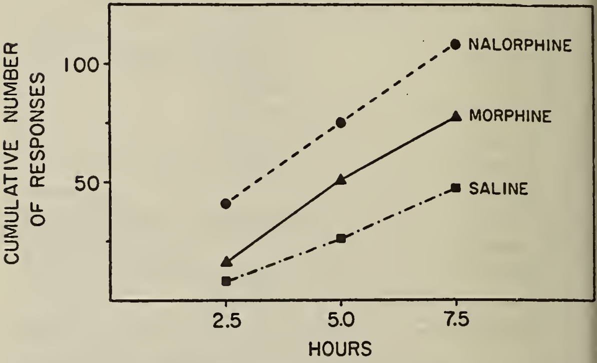
Table 2. Some Signs of Opiate Withdrawal in Opiate-Dependent Rhesus Monkeys*

Gastrointestinal and Autonomic Signs	Motor Activity Signs
Vomiting	Tremors
Retching	Rigidity in extremities
Salivation	Spasticity
Loose stools	Shivering
Coughing	Piloerection
Tachypnea	Holding of abdomen
Dyspnea	
Sweating	Gross Behavioral Changes
Tearing	
Miosis	Yawning and grimacing
Erection and	Restlessness
Masturbation	Screaming (provoked and unprovoked)
	Attacking (provoked and unprovoked)

*Adapted from Villarrel and Karbowski 1974.

These findings have been confirmed and extended by Woods and co-workers (Woods, Downs, and Carney 1975). It was found that, under certain conditions, morphine-dependent monkeys will work to produce the same injection of a narcotic antagonist, naloxone, that they previously worked to avoid. Cumulative records of narcotic antagonist self-administration by a morphine-dependent monkey is shown in figure 3. Each response on an operant manipulandum advances the stepping pen of the cumulative recorder approximately one-quarter of a millimeter and consequently cumulative records provide a direct analog of response rate. Cumulative records of responding on a second-order schedule of reinforcement [FR 10 (FR30:S)] are shown in the top row of figure 3. Every 30 responses produced a secondary reinforcing stimulus (i.e., a 1.5-second flash of light), previously associated with drug infusion, and every 300 responses produced an injection of naloxone (0.002 mg/kg). Antagonist injections were followed by a 1-minute timeout and a light signal. The downward defection on the event marker indicates the delivery of each successive naloxone injection.

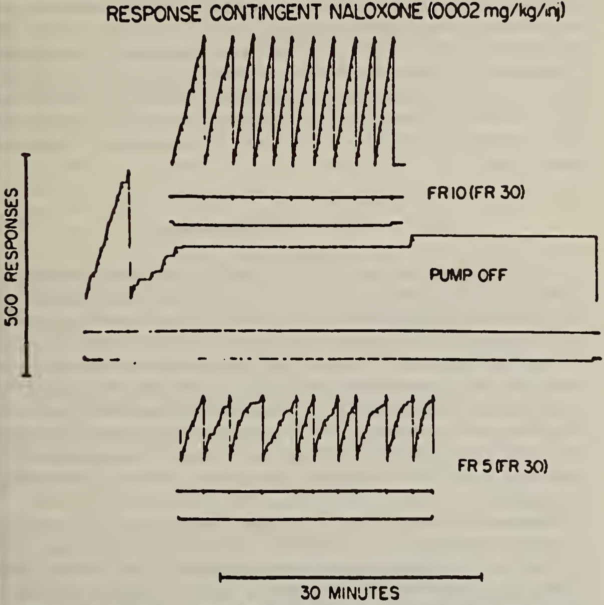
Figure 2. Comparison of Antagonist, Opiate, and Saline Self-Administration by Morphine-Dependent Monkeys



Distribution of responses within the last three saline substitution sessions and nalorphine substitution sessions (100 mcg/kg injection), compared to the distribution of morphine-maintained responses at comparable times on control days. *Abscissa:* Successive 2.5-hour segments of 7.5-hour saline or nalorphine substitution sessions; *Ordinant:* Cumuilative number of responses during successive 2.5-hour segments. Each point represents the mean or results of three sessions with three monkeys. Reprinted with permission, from: Goldberg, et al. 1972. In: *Drug Addiction I. Experimental Pharmacology,* Symposia Specialists, Inc., P.O. Box 610397, Miami, FL. 33161. Copyright 1972 by Symposia Specialists.

It is clear that naloxone, rather than any associated stimuli, maintained responding since removal of naloxone resulted in extinction of response behavior. The second row of figure 3 shows the effect of disconnecting the naloxone infusion pump when the secondary reinforcing stimuli, i.e., the light signal, the timeout, etc.,

Figure 3. Cumulative Records of Responding Maintained by Naloxone in a Morphine-Dependent Monkey



The upper record shows the eighth session of responding when every completed FR 30 unit produced a 1.5-second flash of the house light and every tenth completed FR 30 unit produced an injection of naloxone (0.002 mg/kg per injection) plus a 1-minute time out accompanied by house light illumination. The center record shows performance in the third session, with the naloxone infusion pump disconnected. All other aspects of the procedure were as described above. The lower record shows reinstatement of naloxone-maintained responding in the first session with the naloxone pump reconnected. In this and subsequent sessions, the schedule value was reduced to FR 5 (FR 30). Injections of naloxone or saline are indicated by downward deflections of the center event pen. Each session was terminated after 10 injections or about 1 hour. Reprinted with permission from Woods, J.H., Downs, D.A., and Carney, J. 1975. Behavioral functions of narcotic antagonists: Response drug contingencies. *Federation Proceedings* 34(9): 1777-1784. Copyright 1975 by Federation Proceedings.

remain unchanged. The monkey worked briefly, then stopped responding when no naloxone infusion was delivered. The third row of figure 3 illustrates the reinstatement of naloxone maintained responding during the first session after the naloxone pump was reconnected. The reinforcement schedule requirement was reduced from 300 to 150 responses for each naloxone injection. Under these conditions, morphine-dependent monkeys could earn approximately 10 naloxone injections over the course of an hour. It is apparent that the monkey resumed and maintained responding for naloxone injections.

Electric Shock Self-Administration

The aversive properties of electric shock stimuli have been amply documented. However, a monkey trained to press a key to avoid an intense electric shock can also be trained to press a key to produce an electric shock of the same intensity. In other words, the same electric shock event that can maintain escape and avoidance behavior may, under certain conditions, be self-administered by the same monkey. Identification of this phenomenon, called *response-produced shock*, developed from the initial observations of Kelleher and coworkers (1963) that responding increased during a preshock stimulus, and if the terminal shock was removed, responding decreased.

Response-produced shock has now been observed in many laboratories, across several species, and has been shown to be a reliable and persistent phenomenon (Bacotti 1978; Barrett and Spealman 1978; Byrd 1969; Eubanks et al. 1975; Kelleher and Morse 1968; McKearney 1968, 1969, 1972; Malagodi et al. 1978; Morse and Kelleher 1970; Morse et al. 1977; Morse et al. 1967; Stretch et al. 1968; Stretch et al. 1970). Under certain conditions monkeys will continue to self-administer electric shock for months and even for years. An orderly relationship between shock intensity and responding to produce shock has also been shown (Barrett and Spealman 1978). As shock intensity was increased from 0 to 1, 3, 5, 7, and 10 mA, response rates on a variable interval 3-minute schedule of shock presentation increased from 0.10 to above 0.80 responses per second (Barrett and Spealman 1978).

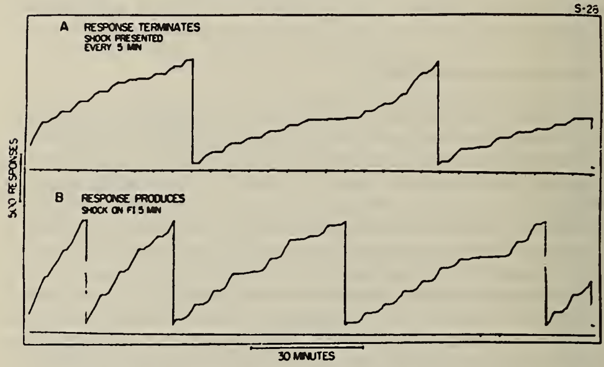
An illustration of behavior maintained by the delivery of electric shock is shown in figure 4 (Morse and Kelleher 1970). Cumulative response records of the operant performance of a single monkey are shown under two different conditions: shock termination and shock production. The top row of figure 4 shows behavior on a schedule of shock termination (FI 5 min) in which the first response after 5 minutes have elapsed terminates a 7 mA electric shock which is presented every 5 minutes. Cumulative responses of the same monkey on a schedule of shock production are shown in the second row of figure 4. Instead of terminating a shock presented every 5 minutes, the monkey self-administers a shock of 1 mA every 5 minutes. If a response did not produce shock within 5 seconds after elapse of the 5-minute fixed interval, a 7 mA shock was presented automatically. It is obvious that the rate of responding was higher when responses produced shock than when responses terminated shock.

Another example of response-produced electric shock is shown in figure 5, which compares the effects of noncontingent and response-produced shock on operant behavior (Morse and Kelleher 1970). In the cumulative record shown at the top of figure 5, a monkey with a particular behavioral history received 5 mA shocks every 2 minutes, independent of his response behavior. Each shock was followed by a brief timeout period. In the lower portion of figure 5, a shock of the same intensity (5 mA) was scheduled to occur after the first response after an interval of 2 minutes had elapsed (an FI 2 min schedule). Shock presentation was followed by a brief timeout. Response behavior was maintained by electric shock presentation. The rate of responding increased and the pattern of responding was more positively accelerated on a shock presentation schedule than when shocks were not contingent on responding (Morse and Kelleher 1970). This basic finding has recently been replicated. Responding increased as the proportion of response-produced shocks increased, but decreased as the proportion of response-independent shocks increased (Bacotti 1978). These data further illustrate the direct relationship between response rate and response-produced shock.

These findings that an animal will work to self-administer a seemingly noxious electric shock, indeed the same electric shock he previously worked to avoid or to escape from, is eloquent testimony to the capacity of "aversive" events to control behavior leading to their self-administration. Morse et al. (1977) have reviewed data on the control of behavior by noxious stimuli and discussed the generality of this phenomenon.

The parallels between these data on response-produced shock and narcotic antagonist self-administration in primates, and the aversive consequences of drug self-administration in humans, are provocative. Although the control of drug self-administration by

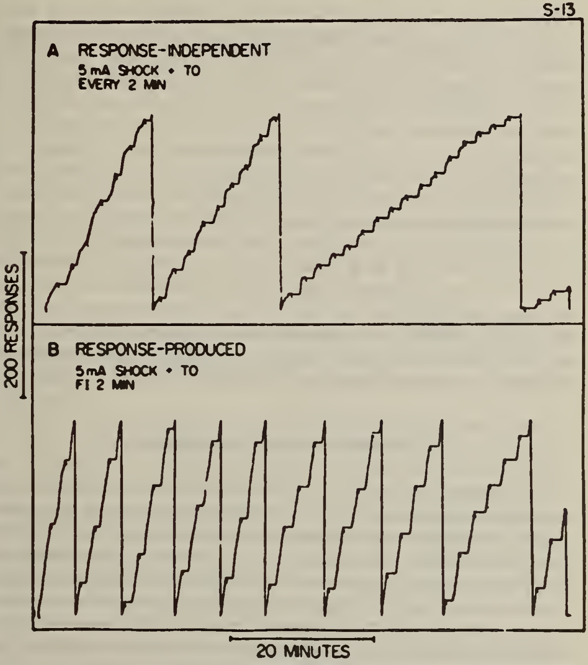
Figure 4. Performance Under an FI 5-minute Schedule of Termination of Electric Shock and an FI 5-minute Schedule of Presentation of Electric Shock (Monkey S-28)



A: Short diagonal strokes in the event record (bottom) indicate successive electric shock presentations (7 ma); diagonal strokes on the cumulative record (top) indicate the termination of shock. B: Strokes on the cumulative record indicate 1 ma electric shock presentations. If a response did not produce shock within 5 seconds after 5 minutes had elapsed, a 7 ma shock was presented automatically. When responses produced shock, rates of responding became higher and patterns of positively accelerated responding became more marked. From Morse and Kelleher 1970. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, N.J. Copyright 1970 by Prentice-Hall, Inc.

aversive consequences has not been shown unequivocally in man with the degree of precision that it has been shown in primate models, the inference that aversive consequences are one part of the reinforcement complex that maintains human drug self-administration behavior is compelling.

Figure 5. Comparison of Performances Under Schedules of Response-Independent and Response-Dependent 5-ma Electric Shocks (Monkev S-13)



Short diagonal strokes on the cumulative records indicate presentation of electric shock; a time out period, in which the paper did not move, followed each shock. The recording pen reset to the baseline whenever 275 responses had accumulated. A: Performance under the schedules of response-independent shock. B: Performance under FI 2-minute schedule of response produced shock after eight sessions. The rate of responding increased, and the pattern of responding was more clearly positively accelerated with response-produced shocks. From Morse and Kelleher 1970. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, N.J. Copyright 1970 by Prentice-Hall, Inc.

Implications of the Control of Behavior by Aversive Consequences

These clinical and experimental data challenge common sense assumptions about what constitutes a "positive" and an "aversive" event and what types of events will be reinforcing. Clearly the physical properties of a stimulus event do not necessarily predict its effects on behavior. In the language of the experimental analysis of behavior, reinforcement is any event that maintains behavior, i.e., a reinforcer is a consequence of behavior that increases the probability of the recurrence of that behavior (Skinner 1938, 1953). Although behavioral scientists are usually careful to distinguish between reinforcement and reward, the terms reinforcing, rewarding, and euphorigenic are often used interchangeably to describe the consequences of drug abuse, and by inference, to explain its recurrence and persistence. The notion of "reward" has a compelling face validity that does not invite critical examination. One advantage of the term reinforcement is that it does not imply anything about the nature of the reinforcing events but, rather, describes a functional relationship between events and behavior.

A Functional Analysis of Behavior

The defining characteristics of reinforcements and punishers are how they change behavior. The same stimulus event may have either reinforcing or punishing effects, depending upon the condition under which it is presented. According to this empirically based formulation, shown schematically in table 3, if the presentation or removal of a stimulus *increases* the behavior leading to that consequence, it can be defined as a reinforcer. If the presentation or removal of a stimulus event *decreases* the behavior leading to that consequence, it can be defined as a punisher (Morse and Kelleher 1977).

Defining stimulus events in terms of their behavioral effects, rather than predicting consequences on the basis of a priori assumptions about the alleged properties of a stimulus event, represents a radical departure from our usual ways of thinking. However, defining stimulus events in terms of actual behavioral consequences is parsimonious and unambiguous. Moreover, it is not necessary to postulate hypothetical constructs, such as motivation, to account for relationships between events and behavior (Solomon 1977). Defining reinforcement and punishment in terms of behavioral effects can account for data on response-produced shock and antagonist self-administration as well as the persistence of drug self-administration which results in aversive consequences during intoxication.

Table 3. Stimulus Events and Their Behavioral Effects

	Behavioral Effect	
Event	Increase Behavior	Decrease Behavior
Present stimulus	Reinforcement	Punishment
Remove stimulus	Reinforcement	Punishment

Electric shock and antagonist self-administration data indicate that it is not the inherent properties of the event, per se, but the way in which the event is scheduled that determines the subsequent effect on behavior (Morse et al. 1977). The reinforcing or punishing properties of stimulus events are dependent upon a variety of factors including the behavioral history of the organism, the schedule of presentation of that event, and the ongoing behavior at the time. Clearly, it is impossible to assume an invariant effect of any particular stimulus event. We have seen that under certain conditions of behavioral history and schedule controls, substances that were so noxious that animals would work to avoid them, undergo a transition from punishing to reinforcing stimuli as a function of the schedule of presentation.

Another striking example of the way in which the scheduling of an event can determine its behavioral effect also comes from research on response-produced shock. Several studies have shown that under multiple schedules of electric shock production and termination, an animal will respond appropriately under each condition within the same experimental session (Barrett and Glowa 1977; Kelleher and Morse 1968; McKearney 1972). Moreover, when a concurrent schedule of variable interval shock presentation and a fixed-interval schedule of shock termination were in effect simultaneously, monkeys responded appropriately on each schedule (Barrett and Spealman 1978). The importance of the schedule of reinforcement in influencing the way in which events control behavior is also illustrated by the demonstration that monkeys will simultaneously respond on a variable-interval 3-minute schedule for cocaine injection *and* on a fixed-interval 3-minute schedule of termination of cocaine availability for 1 minute. Careful controls showed that concurrent termination of cocaine availability and self-administration of cocaine were schedule-specific behaviors which could not be explained by adventitious reinforcement or nonspecific activity increases (Spealman 1979).

Stimulus Self-Administration

Beyond the issue that seemingly "aversive" and "positive" consequences both contribute to the maintenance of drug self-administration, there are many other apparent paradoxes which remain unaccounted for. One example is polydrug use which often involves the simultaneous and sequential use of several drugs with different pharmacological properties and presumably different effects, e.g., stimulants and depressants; opiate analgesics and stimulants. Phencyclidine may be used concurrently with other drugs such as alcohol, barbiturates, or marijuana, each of which has different pharmacological effects and presumably modulates the effect of phencyclidine in different ways.

Some 25 years ago, Wikler and Rasor (1953) wrote that one reason for using drugs advanced by some opiate addicts is to "get off the normal." The nature of the positive effects of drugs described by addicts varies considerably in different types of drug addiction (Wikler and Rasor 1953). Anecdotal accounts of voracious polydrug use, and extreme drug effects produced by agents such as phencyclidine, suggest that the user's goal is to achieve a rapid change in state. The direction of the change, up or down, may be of secondary importance. Accumulating clinical evidence of aversive consequences during drug intoxication also lends credence to a state-change hypothesis. An extreme example is the repeated intravenous injection of phencyclidine to the point of unconsciousness (Fauman and Fauman 1978).

To the extent that simulus change affected by drug use may be more important than any inherently positive or negative characteristics of that stimulus, it may be useful to consider drug self-administration within a more general framework of stimulus self-administration (Mello 1977). Central to the idea that stimulus self-administration is important in the maintenance of drug self-administration is the notion that the stimulus properties of drugs, rather than any specific qualities of the stimuli, may be important determinants of this behavior. State change may be the subjective response to the drug-induced stimulus, whatever that stimulus may be. Perhaps, under some conditions, in individuals with a certain behavioral history, drug self-administration has less to do with the pharmacological properties of the compound, or with its anticipated effects, than with its properties as a definite stimulus event that results in a change in subjective state. This hypothesis implies that any drug which has definite stimulus properties, i.e., behavioral effects for the user, is a drug which has abuse potential.

In conclusion, since consequences which appear to be aversive do maintain behavior leading to their self-administration, more careful attention to the role of "aversive" consequences in human drug self-administration seems indicated. Traditional concepts that drug abuse is maintained primarily as a function of rewarding or euphorigenic consequences are not consistent with the clinical data. Reward-related concepts appear too limited to account for clinically observed consequences of alcoholism and many forms of drug abuse. Moreover, systematic comparisons between types of substance abuse may reveal unsuspected similarities between addictive disorders. This, in turn, may reveal common processes in the genesis and maintenance of substance abuse patterns.

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PROSPECTS FOR A BEHAVIORAL APPROACH TO THE DIAGNOSIS OF THE ALCOHOLIC

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Behavioral assessment is characterized, above all, by (1) emphasis on the direct observation of behavior that can be quantified in a reliable fashion, and (2) a focus on assessment that will contribute directly to treatment planning. The *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association 1980) has only recently addressed the problems associated with reliable observation and recording of behavior and with the relevance of behavior to treatment.

What have behavioral clinicians learned about the behavior of alcoholics to help them plan treatment for alcoholics? Furthermore, what have clinicians discovered about the etiology of the disorder and its course and outcome? Inquiry into etiology, course, and outcome are also legitimate focuses of assessment and diagnosis. This paper reviews the efforts of behavioral researchers and clinicians in assessing alcoholism and its associated behavioral excesses and deficits, in both the laboratory and the real world. The review includes an examination of *DSM III* and National Council on Alcoholism (NCA) conceptions of alcoholism, with an eye to assessing the extent to which they agree with what behavioral researchers have learned about the disorder. The paper concludes with an effort to identify ways in which diagnostic and behavioral assessment can complement each other in the search for more reliable and useful ways of describing the essence of alcoholic behavior for research and treatment purposes.

Behavioral Assessment of Alcoholism and Alcoholics

Behavioral clinicians take a predominantly contemporary view of alcoholism, concluding that much of the behavior of alcoholics stems from immediate environmental influences rather than from historical and psychogenetic factors. This view of alcoholism represents, in large part, a reaction to prevailing psychoanalytic views of the disorder, which see it as a consequence of characterological defects. These defects are presumed to result from crucial negative experiences in early childhood, interacting with the unfolding psychosexual stages. Adding fuel to behavioral assessment efforts are reviews of the psychoanalytic position, which suggest its vulnerability to critical questioning (Hoffman 1976).

One of the most productive behavioral assessment schemas focuses the assessment process on five elements of behavior. Put forth initially by Tharp and Wetzel (1969), the elements describe the pathological behavior itself and the features of the environment in which it occurs that both support and could remediate it. The efforts of behavioral researchers to characterize alcoholism and the behavior of alcoholics fits well within this schema.

1. Measurement of the Frequency, Intensity, and Pattern of the Target Behavior

Assessment of the frequency, intensity, and pattern of drinking by alcoholic persons within controlled laboratory settings was the initial focus of behavioral research on alcoholism. The first laboratory measures of drinking by chronic alcoholics were operant work indexes, reflecting how often alcoholics and nonalcoholics would pull an operant lever—how hard they would work—to accumulate points worth alcohol, social interaction, or other reinforcers (Mello and Mendelson 1965; Mendelson and Mello 1966; Nathan et al. 1970). Many of the alcoholic subjects worked hard enough to earn (and consume) more than a quart of beverage alcohol a day. Their drinking tended to be biphasic in character— a week-long "binge" was typically followed by a much lengthier period of "maintenance" drinking. Four women alcoholics studied in a similar setting (Tracey and Nathan 1976) drank much less than the male alcoholics did, and showed only a "maintenance" pattern of drinking. In these ways, the women more closely resembled four heavy social drinkers studied previously by Nathan and his colleague O'Brien in 1971. More recently, an operant measure of "disposition to drink" in a treatment setting—the amount of work an alcoholic will emit to earn permissible beverage alcohol available to inpatient alcoholics—has been reported to correlate significantly with treatment outcome, suggesting that accurate measurement of the motivation of alcoholics to drink during treatment will help predict their response to the treatment (Funderburk and Allen 1977).

The "taste test," another behavioral assessment method tapping "target behavior," requires subjects to consume alcoholic beverages to rate them along a variety of taste dimensions. The real purpose of the test, however, is covertly to measure alcohol consumption. In an early validation study (Higgins and Marlatt 1973), alcoholics drank more than nonalcoholics of the several alcoholic beverages available in the test, confirming its apparent validity as a measure of alcohol consumption. The predominant use to which the strategy has been put, however, has been to investigate the impact of specific environmental manipulations such as stress induction on drinking. These data are reviewed later in this paper.

Amount and kind of drinking at experimental laboratory bars has also been the subject of behavioral exploration. Schaefer and his colleagues (1971) built the first such bar on the ward of a California State hospital. Observing drinking at the bar, they reported that alcoholics and nonalcoholics drank very differently. Alcoholics tended to gulp straight drinks without ice, and nonalcoholic subjects preferred sipping mixed drinks, to which ice was typically added. New Zealand alcoholics showed essentially the same behavioral differences from nonalcoholics in an experimental bar study in that country (Williams and Brown 1974). The experimental bar featured in Nathan's operant ward (Nathan and O'Brien 1971; Nathan et al. 1970) also documented characteristic differences between the two groups in drinking topography.

Despite the precision, capacity for continuous measurement, and control of key environmental factors that laboratory settings permit, they also lack some of the important environmental and social components of natural drinking settings. For this reason, assessment of drinking behavior in natural environments has also been attempted. After developing appropriate nonobtrusive systems to codify their observations, several investigators, including Cutler and Storm (1975), Kessler and Gomberg (1974), and Reid (1978), observed and recorded drinking by bar and tavern patrons.

Illustrative of this effort to observe drinking behavior when and as it occurs naturally is a recent study by Rosenbluth et al. (1978), who observed the drinking behavior of college students in a university-run beer parlor. Rates of beer consumption varied as a function of sex (males drank more than females), drinking group size (drinkers drank more in groups than in pairs), and group composition (drinkers drank more in the presence of the opposite sex than in same-sex groups).

Despite the promise of these direct behavioral assessment efforts, indirect assessment of drinking behavior is still the more common technique; self-reports of drinking or reports on another's drinking by an informant via questionnaire or structured interview continue to be the most widely accepted source of information. These data sources are easier and cheaper to use, do not require actual alcohol consumption (a problem for "dry" alcoholics), and tap a wider range of data than observational or laboratory measures of drinking. That they yield less reliable indexes of drinking than do direct measures, however, remains a source of concern.

Among the most promising indirect behavioral assessment methods is Marlatt's 19-page Drinking Profile questionnaire (1975), structured to gather data on the same five crucial behavioral assessment components around which this paper is organized. Its section on drinking patterns is especially complete.

Another promising self-report assessment method is the Volume-Pattern Index developed by Bowman et al. (1975). Initially put forth as an alternative to the Volume-Variability Index of Cahalan and Cisin (1968), widely used in Cahalan's influential epidemiologic studies, the Volume-Pattern Index appears better able to describe the variability in drinking patterns so often associated with changes in the functioning of the alcoholic.

Other worthwhile indirect measures of consumption include (1) an 18-item computer-assisted screening interview for alcoholism that includes four questions tapping "symptoms of addictive drinking" (Reich et al. 1975); (2) the Alcohol Use Inventory, a 147-item, 22-scale questionnaire designed to assess pattern, frequency, and intensity of drinking and its consequences, along with setting events and concurrent behaviors (Wanberg et al. 1977); and (3) the Severity of Alcohol Dependence Questionnaire (Stockwell et al. 1979), a 20-item questionnaire that reflects pattern and frequency as well as concomitants of drinking.

To summarize, both direct and indirect behavioral measures of drinking behavior now permit the reliable specification of patterns, amounts, and temporal distribution of drinking for purposes of assessment, diagnosis, treatment planning, and research.

2. Assessment of Antecedent Events: The "Setting Events" for Excessive Drinking

The same direct and indirect behavioral measures of alcohol consumption also have been used to explore the nature of events antecedent to and, probably, causally linked with excessive drinking and its consequences. In a review of this literature, Nathan and Lisman (1976) identified three antecedents of drinking studied most thoroughly by behavioral researchers.

> *Social Interaction Factors*: From research reviewed here (e.g., Bigelow et al. 1974 and 1975; Mello and Mendelson 1965), we now conclude that social interaction facilitates alcohol consumption in most alcoholics. It (also) seems certain that the reciprocal reinforcement value alcohol and social interaction have for each other might well account for much of the marked resistance of the disorder to remediation.
>
> *Interpersonal Anxiety and Social Stress*: The tension-reduction model of alcohol consumption does not receive overwhelming support from the bulk of the experimental literature. The results of studies which favor the model seem more like isolated findings deriving from special stress conditions (e.g., isolated stress, interpersonal stress, retaliative stress [Higgins and Marlatt 1975; Marlatt et al. 1975]) than from conditions which play important tension-inducing roles in the alcoholic's real life beyond the laboratory.
>
> *"Set" and Social Influence*: Studies reviewed provide initial and tentative confirmation for the long-held view that alcoholics as children may in fact have modeled heavy parental drinking behavior just as alcoholics as adults model the drinking behavior of drinking companions.

3. Assessment of Maintaining Stimuli—The Environmental and Cognitive Factors That Reinforce the Target Behaviors

Each of the antecedent events described above as influential in "setting the stage" for alcoholic drinking can also reinforce that drinking after it begins. That is, if the opportunity for social interaction facilitates the likelihood that one will begin to drink, friends also maintain drinking—and extend it. Similarly, if drinking is more likely to begin following the experience of environmental stress, it is as likely to continue in the face of the anxiety and depression that so typically accompany chronic drinking.

Two additional behavioral research programs examining stimuli that maintain alcoholic drinking have recently been reported. The first of these programs concerned itself with the variety of expectancies drinkers and nondrinkers alike share about the reinforcing properties of alcohol, *properties they may not actually experience*. Abrams and Wilson (1979), Marlatt and Rohsenow (1980), and other behavioral researchers (Pliner and Cappell 1974; Wilson et al. 1978) have recently reported that, at moderate blood alcohol levels, both alcoholics and nonalcoholics report that alcohol has reinforcing effects on sexual arousal, response to socially stressful situations, mood, and pain perception, even though a "balanced placebo design" that separates alcohol's pharmacological and expectancy effects indicates that these effects are largely a function of expectancy rather than one of pharmacology. In other words, beliefs in the power of alcohol to change a variety of behaviors from negative to positive may well be as influential in keeping alcoholics drinking as these beliefs are in inducing alcoholics and social drinkers to drink in the first place.

A second new source of data on stimuli that maintain alcoholic drinking stems from the work of Stanford psychologist Rudolph Moos and coworkers (1979), who developed a series of scales to assess the interpersonal and emotional climate of diverse human environments. In a recent study employing Moos' scales, the interpersonal climate of families with alcoholic members in treatment was explored. The climate of families whose members were more likely to benefit from treatment was successfully contrasted with those whose members were unlikely to benefit from treatment by means of a 90-item Family Environment Scale, which measured dimensions like cohesion, expressiveness, and conflict.

Characteristics of successful and unsuccessful alcoholism treatment centers were compared and contrasted in a study using treatment environment scales (Bromet et al. 1976). As important as predicting treatment outcome from family interaction patterns or the interpersonal climate of a treatment facility, the successful development of comprehensive and sensitive scales to reflect environmental and interpersonal factors central to continued alcoholic drinking is more important.

4. Reinforcement Hierarchy—The Range of Factors in the Environment That Reinforce Both Target and Nontarget Behaviors

Besides the large number of diverse reinforcement checklists developed by behavior therapists for use with a wide range of clients (Hersen and Bellack 1976), several groups of behavioral researchers have systematically explored the range of reinforcers capable of moderating excessive drinking by chronic alcoholics. Foremost in this quest is the Baltimore City Hospitals group, including Cohen, Bigelow, Griffiths, Liebson, and their colleagues. Among their findings are (1) an "enriched" (more comfortable, more interesting) living environment is preferred over an impoverished one to the extent that consumption of alcohol by alcoholics is reduced when "moderate" drinking is rewarded with access to an enriched environment, (2) drinking is also reduced when a brief period of contingent social isolation follows consumption of beverage alcohol, (3) opportunity to earn a weekend pass to visit friends or family also leads to moderate drinking when moderation is followed by receipt of the pass (Bigelow et al. 1972, 1976). The same group of researchers, together with Nathan and his colleagues and Mendelson, Mello, and their co-workers, has also reported that opportunity for social interaction leads to a reduction in beverage alcohol consumption when the two factors are contingently linked.

This body of research, then, suggests that, contrary to widespread conviction, alcoholics will moderate their drinking when doing so leads to such reinforcers as social interaction and improved living conditions. Systematic manipulation of these and other reinforcers in the natural environment can, accordingly, contribute to a moderation of drinking by chronic alcoholics. Some open questions persist, however. How long will contingent reinforcement for moderation remain effective for the typical chronic alcoholic? Which of these individuals is most apt to be affected by these environmental contingencies?

5. Potential for Remediation in the Environment

Beyond basic research on contingent environmental reinforcement for moderation, exploration of the potential in the environment for remediation of excessive drinking has been carried on by applied research on comprehensive treatment programs for alcoholics and problem drinkers. Most of these programs attempt to alter drinking patterns by calling on family, friends, employers, and others systematically to withhold or deliver the reinforcers they often provide patients. These efforts strongly suggest that most environments contain a variety of powerful measures for remediation of excessive drinking if appropriate contingencies can be identified and manipulated (Miller and Hester 1980; Nathan and Briddell 1977; Nathan and Lipscomb 1979).

DSM III as a Behavioral Document

The new *Diagnostic and Statistical Manual of Mental Disorders (DSM III)* has been appraised elsewhere (Schacht and Nathan 1977). Several of the substantial changes introduced in *DSM III* will lead to improved diagnostic reliability and utility. Reliability will be enhanced by the specification of operational criteria for each diagnosis. The lists and descriptions of diagnostic cues—generally phrased behaviorally and required for each diagnosis—are largely empirically derived. Thus, they should provide more valid diagnostic categorization. Because each diagnosis is accompanied by a consensually validated set of diagnostic cues (which have been subjected to extensive field testing), reliability will almost certainly be enhanced.

The utility of a *DSM III* diagnosis is also likely to be improved by the advent of multiaxial diagnosis. Coding a patient's behavior on the last two of five diagnostic axes (which call for estimates of the severity of the psychosocial stresses to which the patient was exposed during the past year and of the patient's highest level of adaptive functioning over the same period) ought to help in treatment planning, including assignment to an appropriate treatment modality and choice of an appropriate therapist.

To what extent have these generic improvements in *DSM III* affected the bases for diagnosis of alcoholism? How have the specific changes in diagnostic criteria for alcoholism introduced in *DSM III* affected conceptions of alcoholism? Do other sets of diagnostic criteria (for example, the National Council on Alcoholism criteria) provide a more or less adequate basis for diagnosing and planning treatment for alcoholics? And, finally, to what extent do any of these changes reflect data gathered by and from behavioral researchers?

Alcoholism in *DSM II* was embedded in the personality disorder grouping, which also included sexual deviations and drug dependence. By implication, society held a jaundiced view of alcoholism; it was grouped along with antisocial personality, schizoid personality, homosexuality, and pedophilia. *DSM III* discusses substance use disorders separately, makes no such assumptions, and assigns no such stigma.

DSM III separates the central nervous system consequences of acute and chronic alcohol ingestion from its psychological, social, and physiopathological consequences. The latter are the bases on which the diagnosis of alcoholism in *DSM III* is made. Two diagnoses, alcohol abuse and alcohol dependence, are possible. Operational criteria for alcohol abuse include continuous or episodic use of alcohol for at least 1 month, social complications of use, and either psychological dependence or a pathological pattern of use. Alcohol dependence involves either tolerance, withdrawal symptoms, or both. *DSM III* discusses the typical progression of the disorder, in terms of the appearance of symptoms of abuse or dependence within the first 5 years or regular drinking. The typical pattern of use includes daily intake of large amounts of beverage alcohol, or heavy drinking only during weekends, or long periods of sobriety interspersed with binges of daily heavy drinking lasting for weeks or months. Frequent complications of alcohol dependence include the well-known range of gastrointestinal, hepatic, central nervous system, and cardiac pathology. Depressive symptoms and suicide are considered common accompaniments of the disorder.

DSM III suggests the diagnosis of alcoholism for "patients whose alcohol intake is great enough to damage their physical health, or their personal or social functioning, or when it has become a prerequisite to normal functioning." Alcohol addiction in *DSM II* depended as well on "direct or strong presumptive evidence that the patient is dependent on alcohol, the best direct evidence of such dependence is the appearance of withdrawal symptoms." Inability to go for a day without drinking or heavy drinking for 3 months or more is additional evidence.

Comparing *DSM II* and *DSM III* cues to the diagnosis of alcoholism reveals, then, far greater precision of description in *DSM III*. Moreover, it seems clear that the drafters of this section of *DSM III* drew heavily on behavioral research. Typical variations in patterns of consumption include binge drinking, maintenance drinking, or both, and "pathological patterns of use," including the diverse behavioral consequences of excessive drinking studied by behavioral researchers.

Contrasting *DSM III* diagnostic indexes with those put forth by the National Council on Alcoholism (1972) is also revealing. The NCA criteria, 86 in all, reflect the richness of clinical detail garnered by individuals working with chronic alcoholics over many years; the criteria also reflect NCA's conviction that alcoholism is a physical disease characterized by craving and loss of control and by the inevitable physical and psychological manifestations of the disease of alcoholism. To many behavioral clinicians, the NCA criteria are a mixture of proved and unproved antecedents, consequences, and manifestations of alcoholism.

Although the drafters of *DSM III* chose to define alcohol abuse and dependence with extreme parsimony, the National Council on Alcoholism criteria include 28 major and 58 minor "physiological, clinical, behavioral, psychological, and attitudinal" criteria, further subdivided by diagnostic level of confidence. Reflecting the predominant view of the NCA that alcoholism is a physical disease, these criteria are heavily weighted in the direction of physiological and clinical signs and symptoms of the disorder. Validation studies of the criteria (Ringer et al. 1977) have yielded equivocal results, and critics have questioned the criteria on the basis of the fundamental legitimacy of the unitary label of alcoholism itself (Rohan 1978). Nonetheless, the NCA criteria have stood as the most widely accepted basis for the formal diagnosis of alcoholism until publication of *DSM III*. For that reason, it is surprising that more extensive use of the NCA criteria was not made by the drafters of *DSM III*. This decision seems to reflect both published research (Ringer et al. 1977) and clinical experience to the effect that NCA criteria do not demonstrably add to diagnostic accuracy when compared with the results of using more parsimonious criteria that emphasize signs of withdrawal and tolerance as evidence of physical dependence and social and personal disruption from alcohol for psychological dependence.

DSM III represents, even now, a behavioral approach to the diagnosis of the alcoholic. Diagnostic criteria are phrased behaviorally, in ways that permit operational specification. The criteria are confined to behaviors that have been validated both clinically and empirically, and thus also validate the resulting diagnosis. Explicit decision rules for reliably processing the criteria for diagnostic purposes are provided. What are lacking in *DSM III*, from the behavioral point of view, are the four behavioral assessment elements that complement the target behavior assessment. Even though two diagnostic axes have been added to *DSM III* diagnoses, specifically to increase the utility of the diagnostic process for treatment planning, the resultant diagnostic formulations do not take due account of environmental and interpersonal factors that maintain alcoholism, and that are available to remediate it.

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DISCUSSION OF PAPERS BY LUDWIG, MELLO, AND NATHAN

Roger E. Meyer

The study of behavior and its relationship to alcoholism has been a major research frontier during the past 15 years. Dr. Nancy Mello and her colleague, Dr. Jack Mendelson, have been distinguished pioneers in this work, defining biological, behavioral, and subjective concomitants of intoxicated states in alcoholic subjects, and contributing important new methodology to clinical research in the field. Dr. Mello's hypothesis that the negative feeling states consequent to alcohol and drug abuse may reinforce alcoholic behavior stems from her work with Dr. Mendelson. They found that alcoholics became more anxious and dysphoric as their alcohol intake increased. This observation ran counter to previous hypotheses that alcoholics drank to relieve tension.

Dr. Peter Nathan's work has involved systematic studies of drinking behavior in different populations (males, females, heavy drinkers), with an eye toward identifying environmental conditions associated with differential rates of alcohol intake. He has tried to describe drinking behavior in naturalistic settings and, thus, to precisely define drinking topography (the antecedents and consequences of drinking). He has also studied behavioral methodology, designed to predict treatment outcome in individual patients.

Dr. Mello and Dr. Nathan both come out of the tradition of experimental psychology and its application to operant studies of alcohol consumption in human subjects. In general, this group of investigators has been loathe to talk about terms such as "loss of control" and "craving." They have associated this terminology with a medical disease orientation, which does not permit the possibility that alcoholics can be reeducated into social drinkers by using behaviorally oriented technology. Dr. Arnold Ludwig comes out of a medical tradition, along with his colleague and collaborator, Dr. Abraham Wikler. Dr. Wikler's contributions through the years include studies of drug self-administration in animal models and in humans. His pioneering work led to the research of Dr. Mendelson, and also to the formulations of craving and loss of control described by Dr. Ludwig. The latter's findings represent the most elegant experimental approach to a scientific study of craving. In his introductory remarks, Dr. Ludwig spelled out the polarity between a pure "environmentalist" position and a "restrictive medical disease model." As he states, "The problem with both viewpoints is that they are at the same time both right and wrong; they are right in their emphasis and wrong in their deemphasis." He noted that "disease-oriented approaches have not adequately accounted for environmental and situational factors affecting drinking behavior and, also, the ability of these factors to become conditioned stimuli for alcohol acquisition and consumption." Behaviorally oriented approaches have not taken adequate account of the physiological status of the individual, especially during hyperarousal, as well as the potential "cognitive deficits" that may predispose some individuals to return to heavy drinking.

Despite their differences in scientific background, Dr. Ludwig and Dr. Nathan offer surprisingly similar emphases. For Dr. Ludwig, the most powerful evocation of craving and alcohol acquisition behavior occurs through the combination of appropriate interoceptive and exteroceptive stimuli. If alcohol is consumed in naturalistic settings, one is likely to find far more "craving and alcohol acquisition behavior" than under conditions of placebo administration, or when alcohol is administered in sterile laboratory settings. Dr. Nathan, in turn, emphasizes the importance of specific antecedent "setting events" associated with excessive drinking. These include social interaction factors, interpersonal anxiety and social stress, and factors related to expectancy (set) and setting. Each of the antecedent events sets the stage for alcoholic drinking, and also strongly reinforces that drinking after it begins (according to Dr. Nathan). If social interaction or stressful anxiety facilitates the likelihood that one will begin to drink, drinking is more likely to continue under that condition.

The conflict between these two investigators, then, seems less to do with craving or stimulus control of behavior than it does with the question of "loss of control." Dr. Ludwig argues that alcoholics cannot easily be taught to discriminate their blood alcohol levels, an essential element if one postulates that some alcoholics can be taught to drink in moderate amounts. At Dr. Ludwig's laboratory in Kentucky, 50 percent of the alcoholics (compared with 5 percent of the social drinkers) displayed drinking behavior indicative of loss of control with respect to the task of keeping their blood alcohol levels within a specific socially desirable range. "Loss of control," according to this formulation, represents a kind of feedback dysfunction in which alcoholics are unable to moderate their drinking or to maintain their blood levels within acceptable limits. In contrast, Dr. Nathan cites the work of the Baltimore City Hospital group (as well as his own work), reporting that opportunity for social interaction leads to reduction in beverage alcohol consumption when the two are contingently linked. His findings suggest that alcoholics will moderate their drinking when doing so leads to such reinforcers as social interaction and improved living conditions.

Dr. Nathan's apparent conclusion is that alcoholics can become social drinkers. Dr. Ludwig, in contrast, would argue that although individual psychological, situational, and environmental factors may substantially influence drinking behavior in laboratory settings, the alcoholic who deviates from abstinence is at substantial risk. At this writing, clinical evidence clearly supports Dr. Ludwig's position, although papers by Dr. Linda Sobell and Dr. David Armor suggest that abstinence may not be the only possible positive outcome.

Alcohol has reinforcing, respondent, and discriminative stimulus properties. I believe that the discriminative stimulus properties of ethanol in the blood serve as the most potent trigger for heavy drinking in those with a prior history of heavy drinking. If one believes in stimulus control of behavior, and in the potency of ethanol as a powerful discriminative cue (particularly in the presence of other cues previously associated with heavy drinking), one can appreciate the difficulties faced by the behavior modifier who wishes to convert an alcoholic into a social drinker. The positions of Dr. Nathan and Dr. Ludwig are both theoretically extremely important and have implications for an understanding of the etiology of alcoholism and for its treatment. It would be tragic if the ideological polarities that have marked so much of alcohol treatment also affected clinical research in this field.

In the second portion of his paper, Dr. Nathan described *DSM III* as a behavioral document and pointed out the increased sophistication of the nomenclature. There has been a growing interest in improving diagnostic nomenclature to lead to the identification of prognostically and therapeutically valid diagnostic categories in psychiatry. Approximately 25 percent of alcoholics (probably mostly men) carry the diagnosis of antisocial personality. Twenty-eight to 59 percent of alcoholic patients appear to be depressed. This heterogeneity of psychopathology in the alcoholic population is most interesting.

Organisms have a natural tendency to maintain homeostasis. As a corollary, under conditions of tension or dysphoric hyperarousal, conditions that restore homeostasis are reinforcing. Thus, some theorists have postulated that alcohol is reinforcing as a consequence of its ability to reduce tension. Other theorists have postulated that addicts take drugs to "bind" excessive hostility or anxiety or to relieve depression. Dr. Mello takes a very different position in observing the chronic consequences of intoxication resulting from alcohol, phencyclidine, and heroin. She stated that the ability of the drug to produce a "perceptible state change" may be what reinforces the drug experience. She then cited literature in experimental psychology to demonstrate that aversive consequences can actually be reinforcing under certain reinforcement schedules. Clinicians certainly know of individuals who repeatedly mutilate themselves or slash their wrists, despite obvious aversive consequences. Obviously the environmental context or reinforcement schedule must be important. On hearing of her theoretical formulation initially about a year ago, I rejected it with the idea that one should differentiate between the acute and chronic effects of drugs. Acute administration of alcohol could be reinforcing (each drink could be reinforcing by reducing tension), and the overall state of intoxication could actually be unpleasant. I thought of the unpleasantness as a *mere side effect* of alcohol consumption, rather than as the main source of reinforcement. At greater distance and in the context of the diverse psychopathologies associated with alcoholism, I am convinced that the ability of a drug to produce a perceptible state change—even a negative one—for some individuals, may indeed be reinforcing. This is particularly true for certain individuals with antisocial personality disorders and for some patients characterized as having borderline personality disorders. It is not clear to me that these particular patient groups would modify their drinking for interpersonal reinforcement as described by Dr. Nathan. Indeed the "masochism" of this kind of patient makes that individual particularly resistant to traditional psychotherapies, and particularly difficult to treat.

In viewing these three papers, I am left with a dilemma. I am firmly committed to an abstinence treatment model. I am also committed to understanding more about how to prevent alcoholism and relapse. The three papers demonstrate the extremely rich findings that have come from observing the drinking behavior of alcoholics, yet such studies must remain necessarily controversial and balanced in the context of a favorable risk-benefit ratio. There is a tradition in medicine which may involve risk in order to establish a diagnosis. For instance, it is a cardinal rule that one does not begin treating a patient with an acute abdomen with an analgesic before the surgeon has had an opportunity to establish a diagnosis. The cardiologist may have a patient walk a treadmill to elicit EKG changes that might suggest that the patient is experiencing some ischemia (associated with pain) in the presence of a measured amount of stress. All patients with a history of chest pain are not presumed to have ischemic heart disease. All patients with abdominal pain do not automatically undergo surgery without a careful workup. There has been a problem in the field of alcoholism in that "alcoholics" have been viewed as a homogeneous population. Dr. Nathan cited some of the new questionnaires on drinking typography that may be important to evaluating alcoholic patients. He also cited the potential usefulness of a behavioral paradigm in which alcohol is administered in the assessment of the alcoholic patient in order to predict treatment response.

I would like to end with a series of rhetorical questions:

1. Can you envision a workup evaluation of the alcoholic entering treatment that might include clear and careful behavioral observations of the patient in the presence of ethanol?
2. What are the followup data of subjects who have received alcohol either in research or in treatments that involved videotape confrontation of drinking behavior?
3. Is there evidence that participation in the kind of research that Drs. Ludwig, Mello, and Nathan carried out was in any way harmful or interfered with the individual's later seeking treatment?
4. What should the ethical constraints be on the administration of ethanol to alcoholics?

5. What would the future of alcoholism research be if projects such as those carried out by Drs. Mello, Nathan, and Ludwig could not continue?
6. Can alcoholism treatment advance from knowledge learned from research that involves the systematic study of limited ethanol administration to alcoholic subjects before they are placed in a full treatment program that advocates full abstinence?
7. What can be done to reduce the polarization between behavioral researchers and the treatment community on the issue of the assessment of the alcoholic in the presence of ethanol?

Clearly, the answer to all of these questions must begin with the premise, "Above all, do no harm." I know that we won't have time to answer all of these questions, but I hope that they can serve some useful function. Perhaps we will eventually be able to bring some of the concepts of behavioral analysis into the specific context of our symposium (the evaluation of the alcoholic patient), to improve treatment and to better serve patients.

SESSION V: VARIETIES OF NEGATIVE OUTCOME AND THE PROBLEM OF RELATIVE VERSUS ABSOLUTE RISK

ALCOHOL USE AND THE RISK OF MEDICAL ILLNESS

Robert Scheig

On November 17, 1906, speaking to the Working Men's College, Camden Town, England, Sir William Osler said, "Throw all the beer and spirits into the Irish Channel, the English Channel, and the North Sea for a year and people in England would be infinitely better. It would certainly solve all the problems with which the philanthropists, the physicians, and the politicians have to deal" (Strauss 1968). In the United States in 1978, it was estimated (NIAAA 1978) that 7 percent of the adult population were problem drinkers, and that, in 1975, alcohol abuse and alcoholism drained the economy of about $43 billion annually. Almost $20 billion was attributable to lost production, $12.7 billion to health and medical costs, $5.1 billion to motor vehicle accidents, $2.9 billion to violent crimes, and $0.4 billion to fire losses. At least 14 percent of all patients admitted to the medical service in a general hospital present alcoholism as a significant problem (Nolan 1965) and, in 75 percent of these, the alcoholism contributed to the illness requiring admission. Acute bacterial pneumonia, liver disease, gastritis, pancreatitis, and neurologic disorders were the most common problems. Countless more medical problems are encountered in alcohol abusers by physicians in office practice. This presentation provides an overview of alterations in organ function and the development of disease in humans that appears to be directly related to alcohol consumption.

About 2.7 gallons of absolute ethanol are sold each year in the United States for each person over the age of 14 years (NIAAA 1978). It is estimated that only one-half of the population consumes any alcohol, so ethanol provides an average of 15 percent of the

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daily caloric intake for the drinker, about 525 kcal. The alcohol imbiber often receives fewer calories from food and, with time, may suffer weight loss, signs and symptoms of a wide variety of malnutritional states, vitamin and mineral deficiencies, and diminished serum protein levels, especially albumin. These problems are magnified, of course, in the heavy drinker. Alcohol has also been shown to increase physical requirements for most vitamins, thus compounding the problem.

The gastrointestinal (GI) tract is first exposed to alcohol and may be the organ system that most rapidly reacts to the adverse effects of ethanol. Esophagitis; gastritis; duodenitis; and jejunitis, often with frank ulceration, probably always occur with the consumption of a single large dose of alcohol (Gottfried et al. 1978). The mucosal lesions are often hemorrhagic, and erosions of the mucosa may result in rather brisk upper gastrointestinal hemorrhage. Ethanol probably has a direct toxic effect on the mucosa of the upper GI tract, but it also stimulates gastric acid secretion and delays gastric emptying. Acute intoxication often results in nausea and vomiting, which may progress to retching. Indeed, this condition is the most common setting for the Mallory-Weiss tear. Superficial gastritis is seen in biopsies in more than one-half of chronic alcoholics (Iber 1971). With time, atrophic gastritis, achlorhydria, pernicious anemia, gastric ulcer, and gastric cancer may develop. Alcohol may also be a major contributor to the development of pharyngeal and esophageal carcinoma. All of these effects make alcohol the most common precipitating cause of upper gastrointestinal hemorrhage, and a preventable one.

Ethanol impairs small bowel function and, as a result, malabsorption of a variety of nutrients has been reported. These substances include salt, water, thiamine, folate, ascorbate, B_{12} , xylose, fat, and amino acids (Krasner et al. 1976; Wilson and Hoyumpa 1979). Disaccharidase activity is depressed. Morphological changes in the villi have been noted, including the development of fluid-filled blisters. As a result, diarrhea becomes the rule rather than the exception after either acute or chronic alcohol ingestion; this condition may ultimately result in hypocalcemia, hypomagnesemia, hypokalemic alkalosis, and dehydration. All of these changes are reversible with abstinence.

From time to time, acute pancreatitis has been attributed to the ingestion of a single large dose of alcohol, but except in those instances in which hypertriglyceridemia is present, this correlation has been difficult to establish either in humans or in experimental animals. More commonly, pancreatitis is seen after several years of chronic ethanol consumption. By this time, glandular fibrosis has already occurred, and there is an established chain-of-lakes deformity of the pancreatic ducts, with obliteration of some of the finer radicles (Sarles 1974). The patient may suffer recurrent episodes of pain or be plagued with pancreatic insufficiency, both exocrine and endocrine. The pancreatic insufficiency further enhances malnutrition because of the maldigestion of fat and protein, malabsorption of fat-soluble vitamins, and the presence of diabetes mellitus. There is also suggestive evidence that the development of pancreatic carcinoma is related to chronic alcohol abuse (Burch and Ansari 1968).

Ethanol has profound effects on the liver with respect to the development of disease (Scheig 1970). A single dose and chronic ingestion are quite consistently associated with the development of fatty infiltration of triglycerides in the hepatocyte. Acute alcoholic hepatitis (sclerosing hyaline necrosis of the liver), Laennec's cirrhosis, postnecrotic cirrhosis, hemochromatosis, and hepatoma are all disorders seen with markedly increased frequency in the alcoholic. Even chronic active hepatitis has been reported as one of the alcoholic liver diseases. Because cirrhosis of any type is associated with an increased incidence of gallstone formation, cholecystitis, obstructive jaundice secondary to stone, cholangitis, and pancreatitis all appear more frequently in the alcohol abuser.

The incidence of alcoholic myopathies of skeletal muscle is difficult to ascertain. The myopathy may be subclinical, in which case the diagnosis will rest on finding increased serum levels of enzymes originating in muscle (creatine phosphokinase, lactic dehydrogenase, glutamic oxaloacetic transaminase). The myopathy may be acute, characterized by diffuse muscle weakness or muscle cramps. In severe cases, rhabdomyolysis, myoglobinuria, and the consequent acute tubular necrosis of the kidney may be seen (Perkoff 1971). A chronic form of alcoholic myopathy is also encountered, in which the principal manifestations are proximal muscle weakness, aching, tenderness, and edema.

Cardiomyopathy resulting from alcohol ingestion is not uncommon, and is quite distinct from beriberi cardiomyopathy due to thiamine deficiency. Alcoholic cardiomyopathy usually presents in one of two ways. In the holiday heart syndrome, the patient presents with arrhythmias, premature ventricular contractions, or atrial fibrillation. As the name implies, this condition usually follows a short time of increased alcohol intake and is readily reversible. The other form is much less amenable to therapy, and consists of marked cardiomegaly, a hypokinetic heart, a small pulse pressure but an elevated diastolic one, evidence of peripheral vasoconstriction, and electrocardiogram (EKG) evidence of severe myocardial disease (Ferrans 1966). This condition is apparently due to the effects of alcohol itself and is different from the abrupt onset of left ventricular failure, cardiogenic shock, and acidosis seen in the so-called Quebec beerdrinkers' cardiomyopathy, which was apparently due in part to the addition of cobalt to the beer to improve the magnitude and staying power of the head when poured (Alexander 1972).

There is some evidence that the modest consumption of alcohol, especially in the form of beer, decreases risk of nonfatal myocardial infarcts and death from coronary artery disease (Yano et al. 1977), but there is also evidence that three or more drinks per day increase the risk of hypertension (Klatsky et al. 1977).

The spectrum of neurological sequelae of alcohol ingestion ranges from the acute intoxication syndrome and the hangover to delerium tremens, auditory hallucinosis, Wernicke's disease, cerebellar cortical degeneration, Marchiafava-Bignami disease, and central pontine myelinolysis, which are associated with more chronic abuse (Victor and Adams 1961). Recent evidence indicates that the cerebral atrophy that commonly accompanies chronic alcoholism is partially reversible with abstinence (Carlen et al. 1978). Peripheral neuropathies also develop; these are characterized by delays in nerve conduction, and may affect sensory, motor, and autonomic nerves. Toxic amblyopia is but one specific peripheral neuropathy that may be related to smoking as well as to alcohol ingestion.

In the kidney, there appears to be an increased incidence of renal papillary necrosis in alcoholic patients (Edmonson et al. 1966). Alcohol, by inhibiting antidiuretic hormone, causes water loss. Alcohol also increases calcium and magnesium excretion, but inhibits potassium excretion. The kidney is also affected functionally by end-stage liver disease with the development of progressive azotemia and oliguria, the so-called hepatorenal syndrome. In this disorder, the kidneys are apparently in a hostile environment, but are not themselves diseased—such kidneys have been used successfully as donor kidneys in renal transplants.

The skin is affected by mechanisms not at all understood. Flushing, acne rosacea, rhinophyma, spider angiomata, and liver palms are frequently seen.

Anemia and thrombopenia apparently develop because of a direct toxic effect of ethanol on the bone marrow and are usually rather rapidly reversed by abstinence. These findings are quite distinct from the pancytopenias that result from hypersplenism which results from the portal hypertension that develops with alcoholic liver disease. The anemia may be complicated by folate and B_{12} deficiency. Acute hemolysis, stomatocytosis, target cell formation, and ring sideroblasts may also be seen in alcoholics (Eichner 1973). Leukopenia occurs and there is also a functional defect in the form of inhibited granulocyte adherence and motility, and phagocytic function (Brayton et al. 1970). The increased incidence of infections in the alcoholic may be related to all of the above factors or to lifestyle, aspiration, or the environment of the alcoholic patient.

Numerous endocrine and metabolic abnormalities have been directly attributed to alcohol ingestion. Included in this list are Cushing's syndrome, subnormal T3 levels in euthyroid patients, feminization, hypogonadism, testicular atrophy, impotency, sterility, a diabetes insipidus-like picture, increases in renin and aldosterone levels, lactic acidosis, porphyria, hypoglycemia, hyperglycemia, type IV hyperlipoproteinemia, type V hyperlipoproteinemia, and diabetus mellitus.

Bones are not spared the systemic effects of ethanol; the pathology ranges from osteopenia due to impaired calcium and vitamin D absorption to aseptic necrosis of the femoral head.

Ethanol has an immediate effect on the lung; the drug impairs defense mechanisms against airborne noxious stimuli and also impairs renewal of surfactant. Prolonged ethanol ingestion also causes airway obstruction and limitation of gas diffusion (Heinemann 1977).

This overview does not account for the morbidity and mortality resulting from chronic alcohol ingestion. These are due to increased fetal wastage, the fetal alcohol syndrome, the frequency of automobile and industrial accidents, drowning, fire fatalities, and suicide (NIAAA 1978). The extent of the alcohol-related morbidity and mortality in the United States is shown in table 1.

This paper also does not address the effects of drug overdoses, either those directly caused by alcohol ingestion or those due to the inhibition of the metabolism by alcohol. However, one can paraphrase Sir William Osler's comments regarding syphilis (Strauss 1968) to state, "Know alcoholism in all its manifestations and relations, and all things clinical will be added unto you." Perhaps soon we will also understand how to treat as well as to diagnose alcoholism and its attendant disorders.

Table 1. Percentage of Alcohol-Related Injuries and Fatalities in the United States, 1975

Cause	Injuries	Fatalities
Motor vehicle accidents	33%	50%
Industrial accidents	47	40
Drownings	–	69
Fire	62	83
Suicide	64	37

Taken from: National Institute on Alcohol Abuse and Alcoholism. Third Special Report on the U.S. Congress on Alcohol and Health, from the Secretary of Health, Education, and Welfare, Noble, E.P., ed. DHEW Pub. No. (ADM) 78-569. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1978.

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ALCOHOL, PROTEIN METABOLISM, AND LIVER INJURY*

Charles S. Lieber

Respective Role of Dietary Protein and Alcohol in the Pathogenesis of Liver Injury

Until a couple of decades ago, the interrelationship between alcohol abuse, proteins, and liver injury appeared relatively simple: Protein deficiency was recognized as a complication of alcohol abuse, and protein malnutrition was considered the sole culprit of liver injury in the alcoholic. The following statement, quoted from an authoritative textbook, is fully representative of the prevailing dogma of the time: It was "generally agreed that alcohol is not a hepatotoxin and that its effects on the liver probably are secondary to an associated nutritional disturbance" (Harrison 1958).

This exclusively nutritional theory was plausible since alcoholics do commonly suffer from malnutrition (Korsten and Lieber 1979). Chronic alcohol consumption does indeed interfere with normal food digestion and absorption because of its well-known effects on gut and pancreas. Furthermore, alcohol, high in caloric value,

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* Originally published in Gastroenterology 79:373-390, 1980. Minor editorial changes have been made. Copyright 1980 by the American Gastroenterological Association.

Some of the original studies summarized here were supported, in part, by the Medical Research Service of the Veterans Administration and grants from the National Institute on Alcohol Abuse and Alcoholism and the National Institute on Arthritis, Metabolism and Digestive Diseases.

displaces other foods in the diet. Each gram of ethanol provides 7.1 calories. Twelve ounces of an 86-proof beverage contains about 1200 calories or approximately one-half of the recommended daily dietary allowance for calories. But, unlike regular food, alcoholic beverages contain few, if any, vitamins, minerals, protein, or other nutrients, and, therefore, the alcoholic's intake of these nutrients may readily become insufficient. Economic factors may also reduce consumption of nutrient-rich food, particularly those containing proteins. Indeed, in some epidemiologic studies, alcoholics reported a history of poor protein intake (Patek, Toth, Saunders, et al. 1975). However, one cannot conclude from such an observation to what extent, if any, the low protein intake contributed to the liver complication or was a consequence of it. Interestingly, in other surveys, alcoholics developed cirrhosis despite an average daily dietary protein intake of 100 g or more (Pequignot 1962), which is about twice the daily recommended level (National Academy of Sciences 1979).

The concept that alcoholic liver injury was exclusively of nutritional origin was also based on experimental studies. In rats, it was shown that alcohol given in the drinking water was not capable of producing liver damage unless associated with a diet deficient in essential nutrients, and it was concluded that "there is no more evidence of a specific toxic effect of pure ethyl alcohol upon liver cells than there is for one due to sugar" (Best et al. 1949). However, rats display a natural aversion for ethanol and under the experimental conditions used, intake is relatively small and blood ethanol levels negligible.

When the alcohol aversion was counteracted by incorporation of ethanol in a totally liquid diet, and the ethanol consumption was thereby increased to 36 percent of total calories (an intake still less than that of many alcoholics), fatty liver resulted despite otherwise nutritious diets (Lieber et al. 1963; Lieber et al. 1965; Lieber and DeCarli 1970*a*). The question was then raised whether lesions more severe than steatosis, particularly cirrhosis, can be produced by alcohol in the absence of dietary deficiencies. Studies in rodents had been unsatisfactory because even when given with a liquid diet, the intake of alcohol in rodents does not reach the level of average consumption in the alcoholic, namely 50 percent of total calories (Patek, Toth, Saunders et al. 1975). Such a level of consumption was achieved in the baboon, again through incorporation of ethanol in totally liquid diets (Lieber and DeCarli 1974). The calories (exclusive of alcohol) were provided by protein (36 percent of total nonalcohol calories), fat (42 percent), and carbohydrate (22 percent). This diet was also liberally supplemented with minerals and vitamins. All of the nutrients were calculated to exceed the normal requirements of the baboon (National Academy of Sciences 1978), with choline being given at twice the level recommended by Foy et al. (1964). The fat and carbohydrate composition of the baboon diet was calculated to mimic an optimal clinical situation in which an alcoholic may be trying to achieve a high protein diet with available natural foods while drinking. In fact, even if the alcoholic tried hard, it would be difficult for him to consume a diet richer in protein than the one administered to the baboons (36 percent of nonalcohol calories). Nevertheless, the baboons developed not only fatty liver, but after 2-5 yr, one-third also had progression of liver damage to cirrhosis (Lieber et al. 1975; Popper and Lieber 1980). It was, therefore, concluded that in addition to dietary factors, alcohol itself plays a key etiologic role in the development of liver injury.

If one can extrapolate from these baboon data to the human situation, it would seem that over the long haul heavy drinkers, even if they make an extra effort to maintain a nutritionally adequate high protein diet, will not necessarily succeed in preventing the development of cirrhosis. Many questions, however, still remain unresolved, particularly the extent to which malnutrition promotes the toxic effect of alcohol. In primates, although some fibrosis was produced with protein deficiency alone, no cirrhosis ever developed, except possibly in one animal (Patek, Bowry, and Hayes 1975). For cirrhosis to develop in primates, dietary conditions were required which are not normally achievable with natural food (such as an association of low protein and a high cholesterol content) (Patek, Bowry, and Hayes 1975; Wilgram 1959). Thus whether nutritional deficiencies may potentiate the alcohol-induced liver damage in the primate has not been as yet determined. In some patients subjected to intestinal bypass for obesity, lesions similar to those present in some alcoholics, namely hepatitis and fibrosis, have occurred (Peters et al. 1975), and it has been concluded that in both situations, a similar pathogenesis, namely malnutrition, may pertain. Such reasoning "by analogy," however, is hazardous, since pathogenesis of the liver lesion after bypass is still unsettled. Even if malnutrition were shown to be the culprit in the latter situation, extrapolation to the alcoholic is not necessarily warranted. It could be argued, for instance, that similar liver lesions have also been engendered by chemical agents in humans (Pessayre et al. 1979), not to mention the previously cited experimental evidence of the production of liver damage after alcohol and an adequate diet. At present, the optimal diet for the alcoholic is not established. Obviously, specific nutritional deficiencies, such as lack of thiamine and folate, should be avoided and when present corrected. Concerning proteins, however, the situation is more complex. In rats, carbon tetrachloride-induced cirrhosis can be prevented by a low-protein diet (Bhuyan et al. 1965). The situation in alcoholic liver injury has not been clarified. Early studies relating beneficial effects of high protein diets (Patek et al. 1948) were uncontrolled. Subsequently, the risk of dietary-induced encephalopathy in cirrhotic patients has become more apparent. Therefore, in the absence of experimental data to the contrary, high protein diets do not seem indicated at the present time. Until this issue is resolved it may be prudent to settle for an intake of proteins that does not exceed the recommended amount (National Academy of Sciences 1979), or the individual protein tolerance of the cirrhotic, whichever is lower.

The demonstration of the hepatotoxicity of ethanol raises the question of the mechanisms of this action. The large caloric load that ethanol represents in the alcoholic has been alluded to before. Furthermore, only 2-10 percent of the ethanol absorbed is eliminated through the kidneys and lungs. The rest must be oxidized in the body, principally in the liver, which contains the bulk of the body's enzymes capable of ethanol oxidation. This relative organ specificity probably explains why ethanol oxidation produces striking metabolic imbalances in the liver. These effects are aggravated by the lack of feedback mechanism to adjust the rate of ethanol oxidation to the metabolic state of the hepatocyte, and the inability of ethanol, unlike other major sources of calories, to be stored or metabolized to a significant degree in peripheral tissues. When ethanol is present, it becomes the preferred fuel for the liver. By displacing up to 90 percent of all other substrates normally utilized by the liver (Lundquist et al. 1962), ethanol literally takes over the intermediary metabolism of the liver. The main pathway for ethanol metabolism in the liver proceeds via alcohol dehydrogenase (figure 1). Ethanol loses hydrogen and is oxidized to acetaldehyde, and, as discussed subsequently, each of these two products is directly responsible for a variety of metabolic alterations, including abnormalities of protein metabolism and the development of liver injury.

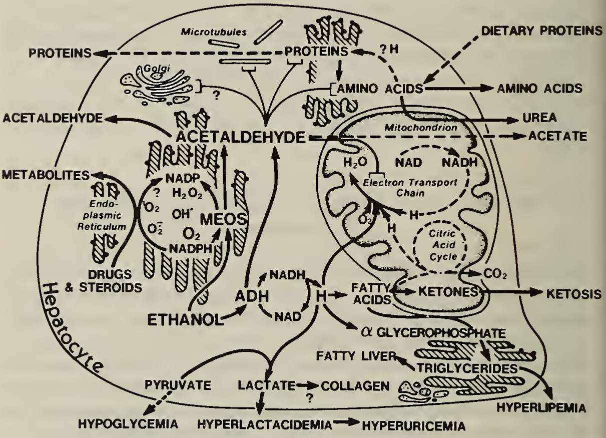
Effects of Excessive Hepatic NADH Generation

As shown in figure 1, the oxidation of ethanol results in the transfer of hydrogen to NAD. At blood levels commonly achieved by drinking, hydrogen generation exceeds the capacity of the liver for hydrogen disposition. The altered redox state (characterized by an enhanced NADH/NAD ratio), in turn, produces a change in the flux of those substrates that are dependent on the NADH-NAD couple for reduction. It was therefore proposed that the altered NADH/NAD ratio is responsible for a number of metabolic abnormalities associated with alcohol abuse (Lieber and Davidson 1962).

Alterations in Intermediary Metabolism, Lipids, and Carbohydrate

The enhanced NADH/NAD ratio is reflected by an increased lactate/pyruvate ratio that results in hyperlactacidemia (Lieber, Jones, Losowsky et al. 1962; Lieber, Leevy, Stein et al. 1962), because of both decreased utilization and enhanced production of lactate by the liver. The hyperlactacidemia contributes to acidosis and also reduces the capacity of the kidney to excrete uric acid, leading to to secondary hyperuricemia (Lieber, Jones, Losowsky et al. 1962). Alcohol-induced ketosis may also promote the hyperuricemia (Goldfinger et al. 1965). The latter may be related to the common clinical observation that excessive consumption of alcoholic beverages frequently aggravates or precipitates gouty attacks (Newcombe 1972). A fascinating, but as yet hypothetical, consequence of the increased availability of lactate may be the stimulation of collagen production and increased hepatic collagen proline hydroxylase activity which conceivably play a role in collagen accumulation (vide infra) (Feinman and Lieber 1972). Furthermore, the altered redox state may also contribute to the hypoglycemia through impairment of gluconeogenesis from amino acids (Freinkel and Arkey 1966), though the latter effect depends on the mixture of amino acids present (Krebs et al. 1973). Urea formation can be diminished by ethanol under these conditions (Stubbs and Krebs 1975), but the mechanism of this effect is unknown. The increased NADH/NAD ratio also raises the concentration of alpha-glycerophosphate (Nikkila and Ojala 1963), that favors hepatic triglyceride accumulation (Johnson 1974) by trapping fatty acids. Some reducing equivalents can be transferred into the mitochondria by various "shuttle" mechanisms. However, the activity of the citric acid cycle is depressed, as discussed elsewhere (Lieber and DeCarli 1977). The mitochondria will therefore use the hydrogen equivalents originating from ethanol, rather than from oxidation through the citric

Figure 1. Oxidation of Ethanol in the Hepatocyte



Oxidation of ethanol in the hepatocyte and link of the two metabolites (acetaldehyde and H) to disturbances in intermediary metabolism, including abnormalities of amino acid and protein metabolism. NAD denotes nicotinamide adenine dinucleotide; NADH reduced NAD, NADP nicotinamide adenine dinucleotide phosphate; NADPH-reduced NADP; MEOS, the microsomal ethanol-oxidizing system; and ADH, alcohol dehydrogenase. The broken lines indicate pathways depressed by ethanol. The symbol denotes interference or binding by the metabolite.

cycle of two carbon fragments derived from fatty acids. Thus, fatty acids that normally serve as the main energy source for the liver are supplanted by ethanol. Decreased fatty acid oxidation by ethanol has been demonstrated in liver slices (Lieber and Schmidt 1961), perfused livers (Lieber et al. 1967), isolated hepatocytes (Ontko 1973), human liver biopsy tissue (Fischel and Oette 1974), and in vivo (Bloomstrand et al. 1973). This results in the deposition in the liver of dietary fat, when available, or fatty acids derived from endogenous synthesis in the absence of dietary fat (Lieber and Spritz 1966; Lieber et al. 1966; Lieber et al. 1969; Mendenhall 1972), and can be considered a major cause for the development of alcoholic fatty liver, the first stage of alcoholic liver injury.

Once a fatty liver has developed, however, fat accumulation does not increase indefinitely, even though alcohol consumption may be continued (Lieber and DeCarli 1970*a*). If the ethanol-induced redox change plays a major role in fat accumulation in the liver, one would expect that the redox alteration becomes attenuated at the time the fat accumulation stabilizes. This was, indeed, found to be the case: In rats fed alcohol chronically, the redox change produced by an acute dose of ethanol in the liver was attenuated after chronic ethanol administration (Domschke et al. 1974). Similarly, in baboons fed alcohol chronically, the redox changes induced by alcohol (as measured by inhibition of galactose metabolism) progressively decreased after chronic ethanol consumption (Salaspuro and Lieber 1979*a*). In the latter experimental model, chronic alcohol consumption is associated with the progression of alcoholic liver injury beyond the fatty liver stage (Lieber et al. 1975). It is apparent, therefore, that although the alcohol-induced redox change may play an important role in the initial development of the alcoholic fatty liver, progression beyond the fatty liver stage must be attributed, at least in part, to mechanisms other than the redox alteration, which will be discussed subsequently.

Alterations in Protein Synthesis

We now realize that in addition to changes in carbohydrate and lipids, the abnormal redox state may also affect protein metabolism.

Effects in Vitro. Acute Changes.

There is a widely held belief that acute ethanol administration inhibits the synthesis of both constituent and export proteins of the liver. This opinion is supported mainly by experimental evidence that has been obtained after addition of ethanol to various in vitro preparations, such as perfused livers (Rothschild et al. 1971; Kirsch et al. 1973; Chambers and Piccirillo 1973; Morland 1975; Oratz et al. 1976), liver slices (Perin et al. 1974; Sorrell, Toma, Schafter et al. 1977), isolated hepatocytes (Jeejeebhoy et al. 1975; Morland and Bessessen 1977). microsomes (Renis et al. 1975), mitochondria (Renis et al. 1975; Rubin et al. 1970; Burke et al. 1975), and ribosomes (Kuriyama et al. 1971; Perin and Sessa 1975); the effect of ribosomes was demonstrated in the membrane bound, but not in the free (Khawaja and Lindholm 1978). Some of these effects may be explained by the fact that various in vitro preparations become deficient in substrates for the hydrogen-translocation shuttles during preparation (Crow et al. 1977), particularly if obtained from fasted animals (Williamson et al. 1974; Meijer and Williamson 1974). Substrates may be diverted away from protein synthesis either because of "leakiness" of the in vitro preparation, or because as suggested by Perin and Sessa (1975) the excess of reducing equivalents generated by ethanol in the cytosol may promote utilization of pyruvate and amino acids for the operation of the shuttles needed to transport the reducing equivalents into the mitochondria. These interpretations are consistent with the aggravation of the inhibitory effects of ethanol by fasting (Rothschild et al. 1971; Kirsch et al. 1973; Jeejeebhoy et al. 1972), the prevention with massive supplementation of amino acids (Rothschild et al. 1971; Kirsch et al. 1973; Perin and Sessa 1975; Jeejeebhoy et al. 1972), pyruvate (Chambers and Piccirillo 1973; Perin and Sessa 1975), or other substrates for the hydrogen-translocation shuttles, especially those of the malic-aspartic acid shuttle (Perin and Sessa 1975; Baraona et al. in press).

Prevention of the inhibition of protein synthesis was also achieved by reducing the shift of cytosolic redox state with an acceptor of reducing equivalents (methylene blue) (Baraona et al. in press). It is possible that the marked shift of the cytosolic redox state may directly affect ribosomal protein synthesis. It has been noted that the addition of ethanol to perfused rabbit livers produces disaggregation of both free and bound polysomes, and detachment of ribosomes from the rough endoplasmic reticulum (Rothschild et al. 1971; Rothschild et al. 1974). This alteration is prevented by inhibiting ethanol oxidation and the associated redox changes with

4-methylpyrazole (Oratz et al. 1978). In regard to all these experiments, it must be pointed out that some degree of anoxia is almost unavoidable in in vitro preparations, and anoxia has been shown to enhance the toxic effects of ethanol on protein synthesis (Jeejeebhoy et al. 1978). In addition, the redox changes produced by ethanol in vitro are much greater than in vivo (Baraona et al. in press): The addition of ethanol in vitro increased the lactate/pyruvate ratio 13-fold, whereas the administration of ethanol in vivo increased this ratio only two times (Domschke et al. 1974). Moreover, the change of the ratio in vitro was essentially due to a marked decrease in the concentration of pyruvate, while a more moderate decrease in pyruvate with a corresponding increase in lactate is observed in vivo. These abnormalities in the lactate/pyruvate ratio have been also found in perfused livers (Rothschild et al. 1971) and liver slices (Sorrell et al. 1977), in association with ethanol-induced inhibition of protein synthesis. Clearly, the in vitro observations referred to above do not pertain to the conditions prevailing in vivo in the well-nourished rat, in which similar ethanol concentrations do not inhibit protein synthesis (vide infra). Actually, it would be of great interest to identify in vivo conditions that mimic the alterations of ethanol metabolism occurring in isolated liver preparations and that induce inhibitory effects of ethanol on protein synthesis. Indeed, under such conditions, the toxicity of ethanol should be greatly enhanced.

Effects of Chronic Ethanol Consumption

Whatever their mechanism, the acute effects of ethanol on hepatic protein synthesis in naive rats may not pertain to the conditions prevailing in alcoholics or in animals in which metabolic adaptations have developed in response to prolonged alcohol exposure. Indeed, ethanol failed to inhibit amino acid incorporation into cell protein when hepatocytes were obtained from rats fed alcohol-containing diets for several weeks (Baraona et al. in press). These hepatocytes also displayed small changes of the lactate/pyruvate ratio in the presence of ethanol. The decreased effect of ethanol in these hepatocytes compared with those in naive pair-fed controls could be due to attenuation of the redox change after chronic alcohol consumption, as reported in vivo in rats (Domschke et al. 1974), in baboons (Salaspuro and Lieber 1979*b*), and in humans (Salaspuro and Kesaniemi 1973). Theoretically, there could also be an increased availability of shuttle substrates. A comparable dissociation between the acute and chronic effects of ethanol on protein synthesis has been reported in vitro in isolated mice ribosomes (Kuriyama et al. 1971) and rat microsomes (Renis et al. 1975); after an acute dose of ethanol these organelles, when obtained from animals fed ethanol chronically, exhibit an enhanced ability to incorporate amino acids into protein, whereas the opposite effect is observed in naive animals. In another study (Khawaja and Lindholm 1978), chronic alcohol feeding to rats more than doubled the ability of free ribosomes to incorporate labeled amino acids. With regard to the effects of chronic alcohol administration on the protein synthetic capacity of bound ribosomes there are apparent discrepancies in the literature. While Renis et al. (1975) found increased leucine incorporation by microsomes (which contain bound ribosomes) of ethanol-fed rats, Khawaja and Lindholm (1978) found a 25 percent decrease in the incorporation of a labeled amino acid mixture (but not of labeled phenylalanine) into bound ribosomes. Only when these ribosomes were detached from the membranes after treatment with Triton X-100 was an increased ability (similar to that of free ribosomes) demonstrated.

In summary, in naive animals ethanol inhibits protein synthesis in vitro in part because of the redox shift and/or pyruvate depletion. The latter changes, however, are much more striking than those observed in vivo. After chronic ethanol feeding, when the redox change becomes attenuated, the in vitro alterations in protein synthesis also tend to disappear.

Effect in Vivo. Acute Changes.

In vivo, the acute effects of ethanol on amino acid incorporation into protein have been less consistent than those described in vitro. No changes in the synthesis of total liver protein were found after administration of ethanol (3-6 g/kg) to naive rats (Morland 1975; Baraona et al. in press; Seakins and Robinson 1964; Ashworth et al. 1965; Mookerjea and Chow 1969). Decreased hepatic production of export proteins (such as albumin and transferrin) has been demonstrated after acute administration of ethanol (3 g/kg) to the rat in vivo (Jeejeebhoy et al. 1972), but, as discussed subsequently, ethanol affects the secretion of such proteins, and under these conditions, effects on synthesis and secretion may be difficult to dissociate. Indeed, delayed appearance in the plasma of newly labeled albumin and fibrinogen was observed after acute administration of ethanol in vivo (Jeejeebhoy et al. 1972). The same reservation also pertains to the inhibition of the hepatic production of serum lipoproteins reported after acute ethanol administration, especially when high ethanol concentrations are achieved (Dajani and Kouyoumjian 1967; Madsen 1969). However, no changes or even an increase in lipoprotein production were observed with more moderate doses (Seakins and Robinson 1964; Elko et al. 1961; Wooles, 1966; Hirayama and Hiroshige 1970; Baraona et al. 1973; Abrams and Cooper 1976). Hypo- and hyperlipemic effects of ethanol have been produced by varying the dose of alcohol administered (Estler 1973). Thus it is not clear whether the decreased production of plasma proteins is due solely to a defect in synthesis or to a concomitant impairment of secretion (vide infra).

Effects of Chronic Ethanol Consumption

In vivo studies of protein synthesis after chronic ethanol administration have yielded conflicting results. Decreased incorporation of labeled amino acids into liver proteins was found by Banks et al. (1970) in rats fed the ethanol-containing diets described by Porta et al. (1968), and by Morland (1974), and Morland and Sjetnan (1976), after several weeks of administration of a mixture of solid and liquid diets containing ethanol. Furthermore, Morland (1974) showed that livers isolated from alcohol-fed rats have a decreased ability to incorporate amino acids into protein after stimulation with dexamethasone, and reduced activity of enzymes (tryptophan oxygenase, tyrosine aminotransferase) involved in protein metabolism. It is noteworthy that in all these studies there was no fatty liver, hepatomegaly, or significant weight gain after administration of the alcohol-containing diets, suggesting that the ethanol intake may have been relatively low and perhaps associated with some degree of undernutrition.

The effects of chronic alcohol administration on protein synthesis were reassessed by Baraona et al. (1977), using rats that were pair-fed the liquid diets described by Lieber and DeCarli (1970). Ethanol-fed rats developed hepatomegaly and fatty liver and the incorporation of leucine into protein was not decreased. Moreover, as previously reported in other species (Shaw and Lieber 1978*a*), alcohol feeding increased the concentration of leucine (and other branched chain amino acids) in the plasma and even more so in the liver, which diluted the specific activity of the tracer in the amino acid precursor pool. After correction for the dilution of the amino acid pool, the rate of protein synthesis (calculated according to

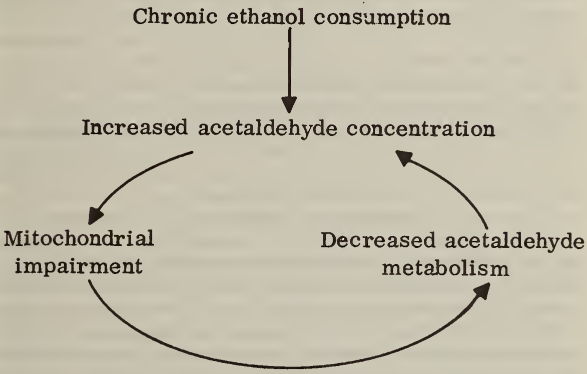
Morgan and Peters (1971*a* and *b*) was found actually to be enhanced after chronic ethanol administration. Similarly, the ethanol-induced inhibition of albumin synthesis that had been observed in naive animals was not reproduced when ethanol was administered to alcoholics (Jeejeebhoy et al. 1975). It is possible, of course, that under special circumstances, such as relative hypoxia or starvation, the redox changes in vivo may approximate those found to be required in vitro to inhibit protein synthesis, but this has not yet been established.

Effects of Acetaldehyde

All known pathways of ethanol oxidation in the liver result in production of acetaldehyde, and it is now generally accepted that more than 90 percent of the acetaldehyde formed from ethanol is in turn oxidized by the liver (Lindros 1974); it is also generally believed that the principal site of acetaldehyde metabolism lies in the mitochondria (figure 2).

Chronic ethanol consumption results in a significant reduction in the capacity of rat liver mitochondria to oxidize acetaldehyde (Hasumura et al. 1976). The decreased capacity of mitochondria of alcohol-fed animals to oxidize acetaldehyde, associated with unaltered or even enhanced rates of ethanol oxidation (and therefore acetaldehyde generation) (Lieber and DeCarli 1970*b*; Lieber and DeCarli 1972) may result in an imbalance between production and disposition of acetaldehyde. Such a mechanism may cause the elevated blood acetaldehyde levels observed after chronic ethanol consumption in rats (Koivula and Lindros 1975), baboons (Pikkarainen, Salaspuro, and Lieber 1979), and humans (Korsten et al. 1975). Recent methodologic advances have revealed that concentrations of "free" acetaldehyde in the blood are lower than the total levels hitherto reported; however, the levels were still higher in alcohol-fed animals than in controls (Pikkarainen, Salaspuro, and Lieber 1979). Levels of acetaldehyde were also elevated in the liver (Baraona, Matsuda, Pikkarainen et al. 1979). The higher acetaldehyde concentrations that result may in turn enhance the functional disturbance of the mitochondria by reducing the activity of various shuttles involved in the disposition of reducing equivalents and by inhibiting oxidative phosphorylation (Cederbaum et al. 1974). The concentrations of acetaldehyde required to achieve the hepatic effects in mitochondria of normal animals were greater than those seen in the blood. However, mitochondria of rats fed ethanol chronically were found to have an increased susceptibility to the effects of acetaldehyde; under these conditions, concentrations of acetaldehyde that could occur in some hepatic compartments were found to depress mitochondrial functions, including lipid oxidation (Matsuzaki and Lieber 1977). Since the rate of ethanol clearance in alcoholics is either equal to or faster than that of nonalcoholics, this "induction" may be the source of greater production of the toxic metabolites (acetaldehyde) resulting in a "vicious cycle." Acetaldehyde causes mitochondrial dysfunction, which in turn promotes higher acetaldehyde levels; this circular process could result in elevation of acetaldehyde and further damage to the liver. Indeed, in view of its reactivity, the increased acetaldehyde can exert a number of adverse effects with regard to protein metabolism and the integrity of the hepatocyte.

Figure 2. Possible Relation Between Ethanol Consumption, Altered Acetaldehyde Levels, and Mitochondrial Impairment


Chronic ethanol consumption
Increased acetaldehyde concentration
Mitochondrial impairment
Decreased acetaldehyde metabolism

Interaction of Acetaldehyde with Amino Acids and Promotion of Lipid Peroxidation

Acetaldehyde has been shown to participate in and to favor the condensation reactions of biogenic amines (Cohen and Collins 1970; Davis and Walsh 1970). Some of the condensation products may be hepatotoxic (Moura et al. 1977). Another possible mode of toxicity of acetaldehyde is its interaction with amino acids. Indeed, aldehydes react quite readily with mercaptans (Schubert 1936; Schubert 1937; Ratner and Clarke 1937). L-Cysteine could complex with acetaldehyde to form a hemiacetal, which would then transform to L-2-methylthiazolidine-4-carboxylic acid (Schubert 1937; Debey et al. 1958). It has been suggested that such a complex may be a nontoxic detoxification product, since cysteine was reported to protect against death from acetaldehyde toxicity in vivo (Sprince et al. 1974). Cysteine, in vitro, afforded protection against the depression of CO_2 production from palmitate, octanoate, and alpha-ketoglutarate by acetaldehyde (Cederbaum and Rubin 1976). On the other hand, cysteine is one of the three amino acids which constitute glutathione. Binding of acetaldehyde with cysteine and/or glutathione may contribute to a depression of liver glutathione (Shaw, Jayatilleke, Ross et al. 1979). Glutathione offers one of the mechanisms for the scavenging of toxic-free radicals; a severe reduction in glutathione favors peroxidation (Wendal et al. 1979), and the damage may possibly be compounded by the increased generation of active radicals by the "induced" microsomes after chronic ethanol consumption.

Indeed, there is a microsomal pathway which requires O_2 and NADPH and which is capable of generating lipid peroxides. Enhanced lipid peroxidation has been proposed as a mechanism for ethanol-induced fatty liver (DeLuzio and Hartman 1967), but its role is still controversial (Hashimoto and Recknagel 1968; Scheig and Klatskin 1969; Bunyan et al. 1969; Comporti et al. 1971). Theoretically, increased activity of microsomal NADPH oxidase after ethanol consumption (Lieber and DeCarli 1970*c*) could result in enhanced H_2O_2 production, thereby also favoring lipid peroxidation.

In any event, it was found that in naive rats, very large amounts of ethanol (6 g/kg) are required to produce lipid peroxidation, whereas a smaller dose (3 g/kg) had no effect. By contrast, after chronic ethanol administration to the rat, even the smaller dose of ethanol administered acutely induced liver peroxidation, and this effect could be prevented, at least in part, by the administration of methionine, a precursor of glutathione (Shaw et al. in press). The ethanol-induced lipid peroxidation was even more striking in the baboon: Administration of relatively small doses of ethanol (1-2 g/kg) produced after 5-6 hr, lipid peroxidation, and GSH depletion. In the baboon chronically fed alcohol (50 percent of total calories for 1-4 yr), fatty liver and, in some, cirrhosis develops; such animals exhibit evidence of enhanced hepatic lipid peroxidation and GSH depletion. These changes were observed after an overnight withdrawal from ethanol and were exacerbated by the readministration of ethanol.

It is tempting to speculate that the propensity of the baboon to develop more severe lesions than the rat after chronic ethanol consumption may in some way be related, at least in part, to the greater susceptibility to glutathione depletion and the initiation of lipid peroxidation.

Interaction of Acetaldehyde with Protein Synthesis

As with ethanol, addition of acetaldehyde to liver inhibits protein synthesis (Perin et al. 1974; Sorrell, Tuma, Schafter et al. 1977; Perin and Sessa 1975; Sorrell, Tuma, and Barak 1977). There is, however, dissociation between the inhibitory effect of ethanol on protein synthesis and the concentration of acetaldehyde. Addition of either aspartate with alpha-ketoglutarate or of methylene blue prevents the ethanol-induced inhibition, despite a marked increase in acetaldehyde accumulations (Baraona, Finkelman et al. 1979). Acetaldehyde oxidation can produce an excess of reducing equivalents and increases the lactate/pyruvate ratio (Forsander 1966). The partial prevention of the acetaldehyde-induced inhibition by supplementation with pyruvate, malate, oxaloacetate, aspartate, etc. (Perin and Sessa 1975), suggests that this inhibition is mediated, at least in part, by changes in redox state due to oxidation of acetaldehyde in the cytosol (in addition to its prevailing oxidation in the mitochondria). Moreover, while the inhibition of protein synthesis, produced by acetaldehyde in concentrations of 320-660 μM is irreversible (Sorrell, Tuma, and Barak 1977), that produced by ethanol is reversible (Perin and Sessa 1975), suggesting that different mechanisms may be involved. Other differences between the effects of ethanol and those of acetaldehyde on protein synthesis have also been reported (Oratz et al. 1978).

Thus, several consequences of ethanol metabolism can be incriminated in the pathogenesis of the ethanol-induced inhibition of protein synthesis in vitro, namely, a marked shift in cytosolic redox state, high acetaldehyde, and low pyruvate concentrations. Metabolism of acetaldehyde may, in turn, exacerbate the redox change. However, neither of these changes has been demonstrated to occur in vivo to the extent required for inhibition of protein synthesis, at least not in well-fed subjects.

Interaction of Acetaldehyde with Protein Secretion

Whereas total protein concentration remains unchanged after chronic ethanol consumption, the concentration of export proteins (such as albumin and transferrin) increases, suggesting an impairment of protein secretion (Baraona et al. 1977; Baraona et al. 1975). Such a secretory defect was further documented, in rats fed alcohol-containing diets, by the observation of delayed appearance of newly labeled albumin and transferrin in the serum with a corresponding retention of these newly labeled proteins in the liver (Baraona et al. 1977; Baraona and Lieber 1977). Acute alcohol administration in vivo to naive rats was also associated with delayed appearance of newly labeled albumin in the serum, retention of labeled albumin in the liver, and increased hepatic content of immunoreactive albumin (Baraona et al. in press). After an acute ethanol dose, the degree of albumin retention was considerably smaller than that of rats chronically fed an alcohol-containing diet (Baraona et al. 1977). Some in vitro studies (Tuma and Sorrell 1977; Sorrell and Tuma 1978) also favor the possibility that the acute inhibitory effects of ethanol are exerted not only on protein synthesis, but on secretion as well. Indeed, 10 mM ethanol (or 340-580 μM acetaldehyde) inhibited the release of prelabeled protein and glycoproteins from liver slices when synthesis was blocked with cycloheximide or puromycin. Other studies in isolated hepatocytes (Morland et al. 1979) did not reveal any inhibitory effects of ethanol on the release of prelabeled proteins. In the latter system, however, colchicine (a potent inhibitor of secretion) decreased protein release by only 27-34 percent, suggesting that this system may lack the sensitivity required to detect the much weaker antisecretory effect of ethanol.

The majority of plasma proteins (with the exception of albumin) are exported from the liver in the form of glycoproteins after glycosylation in the Golgi apparatus. The incorporation of glucosamine into glycoproteins is inhibited by acute ethanol administration both in vivo (Mookerjea and Chow 1969) and in vitro (Sorrell, Tuma, Schafter et al. 1977), suggesting a possible site for the ethanol effect on protein secretion. Ethanol may also inhibit subsequent steps in the glycosylation process, including the final attachment to the protein moiety (Sorrell, Tuma, Schafter et al. 1977). It appears paradoxical, however, that the activity of the glycosyltransferases responsible for the carbohydrate binding to protein at the Golgi apparatus increases already at 16 hr after an acute ethanol dose and even more after chronic ethanol feeding (Gang et al. 1973). Moreover, a defect in glycosylation cannot account for the concomitant impairment in albumin secretion, a protein which does not require glycosylation. Therefore, ethanol must interfere with a secretory step which affects both glycoproteins and nonglycoproteins. Microtubules represent such a likely site. Indeed, drugs (such as colchicine and Vinka alkaloids) that alter microtubules have been reported to impair secretion of macromolecules (such as proteins and lipoproteins) from various organs, including the liver (LeMarchand et al. 1973; LeMarchand et al. 1974; Stein and Stein 1973; Stein et al. 1974; Redman et al. 1975). Reaven and Reaven (1978), who had first questioned the relationship between protein secretion and polymerization of microtubules, now (1980) also find a "tight coupling" between the reduction in hepatic VLDL secretion and hepatocyte microtubule content after the antimicrotubule agents colchicine or vinblastine. In alcohol-fed rats it was shown that the protein export defect was associated with a significant decrease in the content of polymerized tubulin, the major chemical component of microtubules (Baraona et al. 1977). That this biochemical change was indeed due to a decrease in microtubules was then also documented morphologically. The microtubules of ethanol-fed rats were not only decreased in number, but they were shorter and thicker (Matsuda, Baraona, Salaspuro et al. 1979).

Incubation of hepatocytes with ethanol reproduced the microtubular alterations observed in vivo. These effects were prevented by pyrazole, indicating that they were linked to derangements generated by the oxidation of ethanol rather than to ethanol itself. Moreover, serial additions of acetaldehyde to maintain concentrations similar to those reported to occur in vivo ($< 200\ \mu$M) reproduced the effects of ethanol on both polymerized tubulin and visible microtubules. In vivo, the inhibitory effects of ethanol on either microtubules or polymerized tubulin were markedly exaggerated by pretreatment of the animals with disulfiram (an inhibitor of aldehyde dehydrogenase), incriminating acetaldehyde as the principal agent responsible for these effects of ethanol oxidation (Baraona, Matsuda, Pikkarainen et al. 1979). Acetaldehyde (but not ethanol or acetate) binds to tubulin, competes with colchicine for a similar binding site to tubulin, and inhibits polymerization of tubulin isolated from brain (Baraona, Matsuda, Pikkarainen et al. 1979). Inhibition of colchicine binding to liver tubulin by acetaldehyde was also reported by Gabriel et al. (1977).

The disruption of liver microtubules produced by ethanol is associated with engorgement of the secretory vesicles of the Golgi complex (Matsuda, Baraona, Salaspuro et al. 1979), suggesting a concomitant impairment of secretion. Chronic alcohol consumption, which potentiated the disruptive effect of ethanol on microtubules, also enhanced the Golgi engorgement. Conversely, 4-methylpyrazole, which decreased the effect of ethanol on microtubules, also decreased the engorgement of the Golgi. These various observations support the concept that integrity of microtubules is required for normal protein secretion and that the acetaldehyde mediated microtubular alteration is responsible, at least in part, for the impaired protein secretion after ethanol.

Sequellae of Protein Accumulation in the Liver

Effects of Ethanol on Protein Catabolism

It can be calculated from the data of Baraona et al. (1977) that the difference between the rate of synthesis of proalbumin and the rate of release of albumin into the serum should result in an accumulation of albumin far greater than that actually measured. Thus, it is likely that most of the retained proteins undergo degradation. The rate of proteolysis is generally assessed in the liver from the release of branched chain amino acids (leucine, isoleucine, and valine), when reincorporation into protein can be suppressed or accounted for (Khairallah and Mortimore 1970), since these amino acids are not metabolized significantly in the liver (Mortimore and Mondon 1970). Adapting this method to isolated hepatocytes from normal rats, Morland and Bessesen (1977) found no changes in the rate of proteolysis after the addition of ethanol.

These results, however, may not pertain to the conditions of animals fed ethanol chronically, in whom the concentration of branched chain amino acids (such as leucine) increases both in liver and plasma, with a concentration gradient favoring release from liver to plasma (Shaw and Lieber 1978). Preliminary results (Baraona, Shaw, and Lieber 1979) indicate that chronic ethanol feeding increases the turnover of total liver proteins suggesting that the increase in liver leucine (and probably other amino acids) in ethanol-fed rats is due, at least in part, to enhanced protein degradation. Also in keeping with the possibility of increased proteolysis in ethanol-fed animals are the reports of increased urinary nitrogen excretion (Klatskin 1961; Rodrigo et al. 1971). Furthermore, there was an increase in the hepatic content of amino acids, with preferential accumulation of those amino acids that are not normally catabolized by the liver (branched chain amino acids and alpha-amino-*n*-butyric acid). Alpha-amino-*n*-butyric acid (AANB) is a product of methionine, serine, and threonine catabolism. Chronic ethanol administration results in increased hepatic degradation of methionine (Finkelstein et al. 1974). Studies in the rat fed ethanol as 36 percent of total calories revealed increased levels of free AANB in the liver and plasma (Shaw and Lieber 1978; Shaw and Lieber 1980). There was a gradient from liver to plasma suggesting hepatic production. Indeed, experiments in liver slices of ethanol-fed animals demonstrate a 2-3-fold increase in the production of this amino acid (Shaw and Lieber 1980). Increased release from the liver was also shown in baboons fed ethanol as 50 percent of total calories, associated with a striking (sevenfold) increase in plasma AANB after chronic but not acute ethanol consumption; a significant increase in plasma AANB was also found in volunteers given alcohol under metabolic ward conditions (Shaw and Lieber 1978).

Investigations of plasma AANB in alcoholics revealed an increase related to chronic alcohol consumption (Shaw and Lieber 1975). However, the level in the plasma is also decreased by protein deficiency. Indeed, clinical protein malnutrition is associated with characteristic plasma amino acid abnormalities, including depression of branched chain amino acids and AANB (Holt et al. 1968). Furthermore, dietary protein restriction (< 3.5 g nitrogen/day) in college students and adults had been shown to result in depression of branched chain amino acids and AANB (Swendseid et al. 1966; Swendseid et al. 1968). Thus, in alcoholic patients the level of AANB may reflect at least two factors: chronic alcohol consumption, which tends to increase this amino acid, and dietary protein deficiency, which tends to decrease it. In order to use the level of AANB in plasma as a reflection of chronic alcohol consumption it was, therefore, necessary to control for the nutritional factors. Since AANB and leucine are depressed to a similar degree by dietary protein restriction, the level of AANB was expressed relative to the branched chain amino acids of which leucine was selected for convenience. The plasma AANB level relative to leucine was found to be increased in a large number of active alcoholics regardless of dietary protein deficiency or the presence of moderate liver injury (Shaw et al. 1976). This increase was reversible upon cessation of drinking, persisted for days to weeks, did not require the presence of alcohol in the blood and was not present in nonalcoholics with moderate liver injury of viral etiology (Shaw et al. 1976).

Further studies have revealed that the level of AANB relative to leucine is not a linear relation over the range of leucine values and, therefore, replacement of the simple ratio by a normal curve was recommended (Shaw et al. 1978). In addition, determination of GGTP was found to enhance the specificity and sensitivity of the test. In alcoholics with severe liver injury, however, AANB relative to leucine may be increased because of markedly depressed values of plasma leucine and result in false-positive determinations (Shaw et al. 1978; Morgan et al. 1977; Dienstag et al. 1978). However, this group does not usually present a problem with respect to differential diagnosis. Similarly, in patients with extremely severe metabolic abnormalities, such as diabetic ketoacidosis (Felig et al. 1970) massive obesity undergoing starvation (Felig et al. 1969), and subjects consuming an experimental diet with very low carbohydrate and high fat content (Swendseid et al. 1967), the AANB may increase relative to leucine. To exclude such subjects, the simple use of a "dip Stix" test was recommended to detect acetone in the urine (Shaw et al. 1978). It has also been shown that children with Reye's syndrome or a variety of inborn errors of amino acid metabolism may have an elevated AANB (Yudkoff et al. 1979); obviously such children do not constitute a problem in the differential diagnosis and detection of chronic heavy drinkers.

One study reported that alcoholics without liver damage who had been recently drinking did not have elevations in the ratio of AANB to leucine (Morgan et al. 1977). However, recency of alcohol consumption and quantity of alcohol consumed were not specified. Furthermore, this study did not take into account the fact that the relationship of AANB to leucine is not linear over the entire range of leucine values (Shaw et al. 1978). The latter was also a shortcoming of a study of Ellingboe et al. (1978). In experimental animals, the increase in AANB relative to leucine was confirmed after chronic alcohol consumption in the absence of severe liver damage (Stanko et al. 1979).

Although AANB may not offer a practical tool for alcoholism screening in populations which are heterogenous with regard to nutrition and degree of liver disease, there is now good evidence that in rehabilitation programs in which the patient can serve as his own control, measurements of AANB can be particularly useful for documentation of treatment success as well as for the detection of relapses in recovered alcoholics (Shaw, Worner, Borysow et al. 1979). To that effect, it was much more useful than MCV (mean corpuscular volume of red blood cells) and more accurate than gamma-glutamyl-transpeptidase (Ellingboe et al. 1978). For such purposes, the subject's own prior AANB (at discharge) is used for comparison; therefore, no correction of AANB with leucine is needed, and the absolute values of AANB can be usefully interpreted.

Swelling of the Hepatocyte and Possible Relation to Necrosis

Two of the earliest and most conspicuous features of the hepatic damage produced by alcohol are the deposition of fat and the enlargement of the liver. This hepatomegaly was traditionally attributed to the accumulation of lipids. However, in animals fed alcohol-containing diets, it was shown that lipids account for only half the increase in liver dry weight (Lieber et al. 1965), while the other half is almost totally accounted for by an increase in proteins (Baraona et al. 1975). The increase in protein was not associated with changes in concentration, indicating that water was retained in proportion to the increase in protein. The mechanism of the water retention is not fully elucidated, but the rise in both protein and amino acids, plus a likely increase in associated small ions, could account osmotically for a large fraction of the water increase. The increases in lipid, protein, amino acid, water, and electrolytes result in increased size of the hepatocytes. The number of hepatocytes and the hepatic content of desoxyribonucleic acid (DNA) did not change after alcohol treatment, and thus the hepatomegaly is entirely accounted for by the increased cell volume (Baraona et al.

1977; Baraona et al. 1975). There is also an increase in the number of hepatic mesenchymal cells after ethanol feeding (Baraona et al. 1975), but this increase does not significantly contribute to the hepatomegaly. The swelling of the hepatocytes after chronic alcohol administration was found to be associated with a reduction of the intercellular space and with portal hypertension (Israel et al. 1979). Both in rats and baboons fed alcohol, and in alcoholic patients, the swelling is most conspicuous in the centrolobular (also now called perivenular) area, which is the zone with the lowest oxygen tension. It has been postulated that ethanol, through enhancing the metabolic demand, may precipitate hypoxia and aggravate hepatic damage (Israel et al. 1977).

Subcellular Site of Protein Accumulation in the Liver

As discussed before, alcohol consumption results in proliferation of the smooth membranes of the endoplasmic reticulum (Lieber 1973). The increase in microsomal protein, however, accounts for only 30% of the total protein increase. Mitochondria are also grossly altered after alcohol administration (Iseri et al. 1966; Lane and Lieber 1966; Rubin and Lieber 1967). Swollen and giant mitochondria are commonly observed, but total mitochondrial proteins do not contribute significantly to the total increase in liver protein. More than half of the total increase in liver protein is actually due to increased soluble proteins of the cytosol (Baraona et al. 1975).

Type of Proteins that Accumulate in the Liver After Chronic Alcohol Consumption

As discussed before, contrasting to the lack of changes in the concentration of total hepatic proteins, the concentration of some proteins (such as albumin and transferrin), which are primarily destined for export into the plasma, was found significantly increased in the liver of ethanol-fed rats, whereas the concentration of soluble constituent proteins (such as ferritin) decreased (Baraona et al. 1977; Baraona et al. 1975). The increased concentration of export proteins reflects an even greater increase in the amount per total liver since alcohol administration produced hepatomegaly. Conversely, decreased concentration of the other proteins after alcohol feeding may merely reflect dilution in enlarged protein and water pools.

It was shown, in the case of albumin, that the increase involves precursor proteins (such as proalbumin) as well as mature serum albumin (Baraona et al. 1977). The current theory is that proteins destined for export are synthesized by bound ribosomes, discharged into the cysterna of the rough endoplasmic reticulum, and then transported to the smooth endoplasmic reticulum and Golgi apparatus (Morgan and Peters 1971*a*; Morgan and Peters 1971*b*; Peters 1962; Glaumann 1970; Glaumann and Ericsson 1970; Peters et al. 1971; Redman and Cherian 1972). This theory, supported by biochemical evidence, has been disputed in the case of albumin because of electron microscopic evidence that indicates direct discharge of albumin from bound ribosomes into the cytosol (Lin and Chang 1975). Although immuno-reactive albumin accumulates preferentially in the cytosol and transferrin in the microsomal fraction, after ethanol feeding the concentration of these proteins increases in both compartments. Since no evidence of leakage from the microsomes was obtained, the possibility that the cytosol could serve as a storage site of retained proteins had to be considered (Baraona et al. 1977). By immunoelectron microscopy, albumin was found to accumulate in the endoplasmic reticulum but not the cytosol of alcoholics (Feldman and Maurice 1977). In the latter compartment, however, the concentration of albumin may have been too small to be detectable by the technique used. It must also be pointed out that the increases in these two export proteins (albumin and transferrin) account for only a small fraction of the total increase in soluble proteins. Thus, the major contributor to the ethanol-induced accumulation of liver protein has not been identified as yet.

Alcoholic liver damage can also be associated with the formation of Mallory bodies, clusters of fibrillar material that resemble intermediary filaments normally present in various tissues. Although the severity of the lesions is usually somewhat greater in cases with Mallory bodies (Harinasuta and Zimmerman 1971; Christoffersen and Juhl 1971), no significantly worse prognosis was associated with their presence. These Mallory bodies, although helpful in establishing an etiologic diagnosis, are not pathognomonic for alcoholic liver disease. Indeed, similar structures have occasionally been described in primary biliary cirrhosis (MacSween 1973; Gerber et al. 1973), hepatocellular carcinoma (Keeley et al. 1972), Indian childhood cirrhosis (Roy et al. 1971), after perhexiline-maleate (Pessayre et al. 1979) or griseofulvin treatment (Denk et al.

1975), and in patients who underwent bypass operation for morbid obesity (Peters et al. 1975).

The exact nature and pathogenesis of alcoholic hyaline has not been elucidated. These fibrils are morphologically and chemically different from microtubules and from microfilaments (actin) (French et al. 1976) and may represent prekeratin (Denk et al. 1979). However, because antitubulins (such as griseofulvin and colchicine) have the ability to induce the formation of Mallory bodies in mice (Denk et al. 1979; Denk and Eckerstorfer 1977), it is possible that the appearance of these bodies in alcoholic hepatitis may be linked to the antitubulin effects of chronic alcohol ingestion. In any event, Mallory bodies may stimulate some immune responses which have been incriminated by Leevy et al. (1979) in the progression of alcoholic liver injury, but this is still the subject of controversy. Even in the absence of Mallory bodies, one suspects that ballooning and associated gross distortion of the volume of the hepatocytes may result in severe impairment of key cellular functions. In alcoholic liver disease some cells not uncommonly have a diameter which is increased two to three times, and thereby their volume is increased about 4-10-fold. One may wonder to what extent this type of cellular disorganization, with protein retention and ballooning, may promote progression of the liver injury in the alcoholic. Indeed, there are other instances of protein retention in the liver such as alpha$_1$ -antitrypsin deficiency, associated with progression to fibrosis and cirrhosis. By analogy, one may assume that the extent of protein retention may in some way also favor progression of liver disease in the alcoholic.

The present prevailing view is that alcoholic cirrhosis develops in response to alcoholic hepatitis. The latter is characterized not only by ballooning of the hepatocyte, but also by extensive necrosis and polymorphonuclear inflammation. It is understandable that necrosis and inflammation may trigger the scarring process of cirrhosis, but one must question whether this is the only mechanism involved. In some populations, particularly in Europe and Japan (Inoue 1966), cirrhosis commonly develops in alcoholics without an apparent intermediate stage of florid alcoholic hepatitis. This observation raises the question of whether alcohol can promote development of cirrhosis without the latter being preceded by alcoholic hepatitis. Indeed, in baboons fed alcohol, fatty liver developed, the hepatocytes increased in size, and there was some obvious ballooning. This ballooning was associated with some mononuclear inflammation but very few of the polymorphonuclear cells so characteristic of human alcoholic hepatitis (Popper and Lieber 1980). Although some clumping was apparent in the cytoplasm, by electron microscopy there was no alcoholic hyaline. Thus there was no picture of florid alcoholic hepatitis; yet, in one-third of the animals, typical cirrhosis developed. If one can extrapolate from these baboons to humans, it appears that alcoholic hepatitis may not be a necessary intermediate step in the development of alcoholic cirrhosis.

This hypothesis in turn raises the question of which process, in the absence of alcoholic hepatitis, may initiate cirrhosis upon chronic consumption of ethanol. It is possible that cirrhosis develops in the presence of minimal inflammation and necrosis, which may suffice to trigger the fibrosis (Lieber 1977). On the other hand, it is also possible that alcohol may have some more direct effect on collagen metabolism independent of the necrosis and inflammation as discussed subsequently.

Obviously, the mechanisms whereby alcohol abuse leads to necrosis of the hepatocyte have not been fully elucidated. It is likely that a variety of factors are involved, such as toxic effects of acetaldehyde, consequences of injury to the endoplasmic reticulum, mitochondria, and microtubules as well as the physical damage resulting from the accumulation of fat and protein and the distention of the hepatocyte. Whatever its mechanism, recognition of the severity of the necrosis and inflammation may be of clinical import.

Liver biopsy is the most objective way of determining the degree of liver cell necrosis, but this is obviously not a practical tool for routine follow-up of a patient or for mass screening purposes. Therefore, spill-over in the blood of liver enzymes, especially transaminases, is commonly used as a marker of liver cell damage. However, blood transaminase values are a poor reflection of liver cell necrosis as revealed on biopsy (Kallai et al. 1964), especially in alcohol-induced liver cell injury. In alcoholic hepatitis, for example, levels of transaminases are only moderately elevated, and normal values can occasionally be found (Beckett et al. 1961). Gamma-glutamyl-transpeptidase (GGTP) is not more reliable, although some correlation with liver cell necrosis exists (Wu et al. 1976). Elevation from nonhepatic origin is common and in some alcoholics elevated levels may only reflect microsomal induction (Freer and Statland 1977; Ishii et al. 1976; Teschke 1977), although Morland et al. initially questioned the induction, they now confirmed it (1977). In contrast with transaminases and GGTP, which show a considerable overlap between patients with and without significant cell necrosis on biopsy, a recent study found that glutamate dehydrogenase (GDH) more accurately reflected the degree of underlying cell damage (Van Waes and Lieber 1977*b*). The high liver content of this enzyme (Schmidt and Schmidt 1962), its solely mitochondrial origin (mitochondrial lesions associated with alcoholic liver disease have been discussed before) (Matsuzaki and Lieber 1977; Iseri et al. 1966; Labe and Lieber 1966; Rubin and Lieber 1967; Lieber 1977), and its predominantly centrolobular localization (Guder et al. 1975) (the area which suffers the major impact of alcoholic liver injury) could explain the advantage of the enzyme as an index of liver cell damage in alcoholic patients. However, to help define the severity and progressive nature of alcoholic liver injury, the GDH determination must be carried out soon (within 1-2 days) after the alcoholic episode; thereafter, the values drop rapidly, whereas liver necrosis persists. Thus, except for the early stage, GDH offers no advantage over other enzymes (Worner and Lieber in press).

Collagen Accumulation

Cellular injury is associated with extracellular deposition of the collagens, a family of proteins which are now well characterized. In alcoholic liver injury there is a great variability in the magnitude of collagen deposition. At the earlier stages, in the so-called simple or uncomplicated fatty liver, collagen is detectable by chemical means only (Feinman and Lieber 1972; Patek et al. 1976). When collagen deposition is sufficient to become visible by light microscopy, usually it appears first around the central (also called terminal) venules, resulting in so-called "pericentral" or "perivenular" sclerosis. This lesion is usually described in association with full-blown alcoholic hepatitis. Less well recognized is the fact that this pericentral sclerosis can already occur at the fatty liver stage in the absence of hepatitis (Edmondson et al. 1967; Van Waes and Lieber 1977*a*). In a retrospective study of liver biopsies from hospitalized alcoholic patients that had been read by the pathologist as simple fatty liver, appropriate staining disclosed pericentral sclerosis in 40 percent (Van Waes and Lieber 1977*a*). Experimental studies in alcohol-fed baboons show that in those animals which progressed to cirrhosis, pericentral sclerosis invariably occurred already at the fatty liver stage; by contrast, animals that did not show the lesion did not progress beyond the stage of fatty liver. These experimental data suggest that, at least in the baboon, pericentral sclerosis is a common and early warning sign of impending cirrhosis if drinking continues (Van Waes and Lieber 1977*a*). The concept of pericentral sclerosis as a precirrhotic lesion in alcoholics is further strengthened by similar observations in patients with fatty livers after bypass operation for morbid obesity (Marubbio et al. 1976) and in diabetic individuals (Falchuck et al. 1980), and preliminary findings in alcoholics (Worner and Lieber 1978). What initiates the collagen deposition in the perivenular area is not known, but again some clues may be derived from the experimental model of cirrhosis in the baboon. Sequential biopsies in alcohol-fed baboons revealed in some animals already at the early fatty liver stage the appearance in the perivenular central areas of an increased number of lipocytes (Ito cells) or transitional cells between lipocytes and fibroblasts (Matsuda, Worner, and Lieber 1979). Animals with an increased number of Ito and transitional cells eventually underwent deposition of abundant collagen bundles, first in the perivenular areas, leading to perivenular sclerosis and ultimately to diffuse fibrosis and cirrhosis. In cases of alcoholic hepatitis, Kent et al. (1976) previously described an increased number of Ito cells. We now realize that even in the absence of alcoholic hepatitis, and before any fibrosis, some animals show an increased number of these cells, and these are the animals that ultimately progress to fibrosis. Thus, these Ito and transitional cells appear to play a key role in the overabundant deposition of collagen. However, the mechanism for the increase in this protein has not been elucidated, nor do we know the respective role of parenchymal and nonparenchymal cells in the production of collagen.

The accumulation of hepatic collagen during the development of cirrhosis could theoretically be accomplished by increased synthesis, decreased degradation, or both. The rate of hepatic fibrous tissue degradation has never been directly measured in human alcoholic liver disease or in any of the animal models of alcoholic liver disease. Therefore its role in the pathogenesis of hepatic fibrosis is unresolved. Collagen half-life is, however, prolonged in the fibrosis of ethionine intoxication and carbon tetrachloride-induced cirrhosis (Hutterer et al. 1964; Hutterer et al. 1970). The cirrhosis of choline deficiency (to which the rat is highly susceptible and by which primates are much less affected) may be exacerbated in the rodent by administration of ethanol and in this context collagen degradation may be slowed (Henley et al. 1977).

The mechanisms of collagen degradation in the liver are complex. We have recently developed a quantitative assay for neutral collagenase activity in liver homogenate (Okazaki et al. 1977), and preliminary results suggest a paradoxical increase in the activity of this enzyme in animals fed ethanol (Okazaki et al. 1977).

The results observed with lysosomal enzyme activity are, in part, contradictory. After 2 wk of ethanol administration (1 g/kg i.p.) the activities of lysosomal enzymes were decreased (Platt et al. 1971), whereas with larger, oral doses they were unchanged after 1 mo and increased after 6 mo (Mezey et al. 1976). Henley and Laughrey (1979) reported that in ethanol-treated rats inhibitors directed toward lysosomal peptidases (tested against radioactive collagen substrate at pH 4) are increased.

Chronic ethanol consumption with adequate diets led to accumulation of hepatic collagen in rats and baboons, even when fibrosis was not yet histologically detectable (Feinman and Lieber 1972). In the latter model, the role of increased collagen synthesis is suggested by increased activity of hepatic peptidylproline hydroxylase in rats and primates and increased incorporation of (^{14}C)proline into hepatic collagen in rat liver slices (Feinman and Lieber 1972). The role of increased collagen synthesis has been confirmed indirectly in humans by autoradiographic techniques utilizing liver biopsies (Chen and Leevy 1975). Using a slightly different alcohol feeding technique for rodents, which did not result in the expected hepatomegaly, Mezey et al. (1977) were able to demonstrate hepatic mechanism. A possible mechanism whereby alcohol consumption may be linked to collagen formation is the increase in tissue lactate secondary to alcohol metabolism (Feinman and Lieber 1972). Elevated concentrations of lactate have been associated with increased peptidylproline hydroxylase activity both in vitro (Green and Goldberg 1964) and in vivo (Lindy et al. 1971). The hepatic-free proline pool size, which has been incriminated in the regulation of collagen synthesis (Rojkind and DeLeon 1970; Chvapil and Ryan 1973), may be increased by ethanol (Hakkinen and Kulonen 1975), and is expanded in human portal cirrhosis (Kershenobich et al. 1970). Recently, it has again been postulated that lactate may play a role (Kershenobich et al. 1979) this time through inhibition of proline oxidase (Kowaloff et al. 1977). This hypothesis illustrates once more the possible impact of ethanol-induced redox changes on intermediary metabolism, including metabolism of protein, and in particular, collagen. Further studies, however, are needed to elucidate all mechanisms involved as well as to resolve some other important, but as yet unexplained effects of ethanol, such as its possible interference with hepatic regeneration: Whereas some found no effect on regeneration (Craig 1975; Frank et al. 1979), others (Wands et al. 1979) report inhibition of (^{3}H)thymidine incorporation but offer no explanation.

In summary, there are two mechanisms which play a major role in mediating the effects of ethanol on intermediary metabolism, including protein metabolism and liver injury. Ethanol is oxidized in the liver to two products (hydrogen and acetaldehyde) to which many of the effects of ethanol can be attributed. The hydrogen generation alters the redox state; and, although this effect is attenuated after chronic ethanol consumption, it may still be sufficient to explain alterations in lipid and carbohydrate metabolism, possibly increased collagen deposition, and, under special circumstances, depression of the synthesis of protein whereas secretion of proteins is affected by acetaldehyde. It is noteworthy that after chronic consumption of ethanol, acetaldehyde is increased, in part, because of decreased oxidation in the mitrochondria, and, partly because of induction of an alternate pathway of ethanol metabolism, namely the microsomal ethanol-oxidizing system. Increased acetaldehyde is associated with impaired microtubules, protein retention, and swelling of the hepatocyte. Acetaldehyde also exerts toxicity with regard to other key cellular sites; it interferes with oxidations in the mitochondria, and it may promote peroxidation of cellular membranes. Hepatocellular injury is followed by extracellular collagen deposition, but what eventually attracts an increased number of lipocytes and fibroblasts and promotes fibrosis is not known. Alcoholic hepatitis, when present, can obviously trigger fibrosis, but the cirrhotic process occurs even in the absence of florid alcoholic hepatitis. Cirrhosis can develop despite an associated adequate diet. However, decreased intake of dietary protein or decreased absorption of amino acids derived from dietary protein may contribute to the depletion of amino acids in the liver which, in turn, may potentiate the toxicity of alcohol.

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CENTRAL NERVOUS SYSTEM IMPAIRMENT IN THE ALCOHOLIC: A RESEARCH AND CLINICAL PERSPECTIVE

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The incidence of brain dysfunction in sober alcoholics obviously varies as a function of selection criteria. However, it has been estimated to range from 50 to 60 percent in alcoholism treatment programs that do not screen for central nervous system (CNS) impairment (Parsons 1977). Brain functioning in alcoholics is therefore a clinically relevant area of research and has been the subject of much study and concern. This paper documents the presence of CNS impairment in alcoholics, discusses possible etiological factors related to this impairment, and assesses whether improvement in functioning is associated with subsequent abstinence. In addition, some of the clinical concerns regarding brain dysfunction in alcoholics are discussed, including (1) admission to alcoholism treatment programs and subsequent rehabilitation efforts, (2) indecision as to whether treatment should begin immediately after detoxification or after short-term improvement, (3) relationships between CNS functioning and treatment outcome, and (4) neuropsychological consequences of posttreatment alcohol consumption.

CNS Impairment

The three basic approaches used to investigate brain structure and function in alcoholics are anatomical, electrophysiological, and neuropsychological. Correlations between physical deterioration of portions of the CNS and alcoholism have been demonstrated by computerized tomography (Fox et al. 1976; Von Gall et al. 1978; Cala et al. 1978; Carlen et al. 1978; Gall and Becker 1948), pneumoencephalography (Tumarkin et al. 1955; Haug 1968; Carlsson et al. 1970; Ferrer et al. 1969; Brewer and Perrett 1971), and neuropathological examination (Courville 1955; Neuburger 1957; Lynch 1960; Victor et al. 1961; Poser 1973). Cortical atrophy, particularly involving the frontal lobes, is the most common finding. Other areas of abnormal CNS structure include parietal and temporal cortices, cerebellum, and the subcortical lesions associated with the Wernicke-Korsakoff syndrome.

Electroencephalographic (EEG) assessment of the alcoholic has detected abnormal electrical activity in the brain, consisting of low voltages and an increased percentage of medium-rapid and beta waves in frontal and parietal regions, and an unusually large amount of slow activity in frontotemporal regions (Bennett et al. 1956; Hudolin 1967; Hudolin and Gubarev 1967). In addition, alterations in the alpha rhythm, as well as poorly developed alpharhythm blocking responses, have been observed (Hudolin 1967; Hudolin and Gubarev 1967). Even though these abnormal electrical responses have been reported to occur in alcoholics, many investigators have not found EEG assessment useful in detecting brain dysfunction (Brewer and Perrett 1971; Begleiter and Platz 1972). However, sensory-evoked potentials in sober alcoholics appear to be differentiable from those of normals (Coger et al. 1976; Knorring 1976), and this technique of assessing brain function may prove to be of future value.

One of the initial attempts to link neuropsychological deficits with the use of alcohol involved the administration of intelligence tests to alcoholics. These studies have been reviewed critically, and it has been concluded that there is no justification for viewing the alcoholic as a person possessing overall intellectual impairment (Kleinknecht and Goldstein 1972; Matarazzo 1979). However, alcoholics do have demonstrable deficits in motor performance, perceptual capacities, conceptual shifting, visual-spatial abstracting abilities, and memory function (Kleinknecht and Goldstein 1972; Goodwin and Hill 1975; Tarter 1975; Grant and Mohns 1975; Eckardt et al. 1978), and therefore perform similarly to people with organic brain damage (Fitzhugh et al. 1960, 1965; Jones and Parsons 1971, 1972; Smith et al. 1973). Many of the psychometric tests commonly used to assess alcoholism-associated brain dysfunction have been found valid (Reitan 1966; Matarazzo 1972) and clinically reliable (Matarazzo et al. 1973, 1976). Typical examples of neuropsychological performances obtained from 116 drug-free alcoholics are shown in table 1. On many of these tests, mean performance was at levels indicative of brain dysfunction.

It is concluded that the evidence from these anatomical, electrophysiological, and neuropsychological studies documents conclusively that alcoholics have CNS impairment. It is also apparent that the detection of this dysfunction is dependent, in part, on the assessment procedure used. Many of the clinical issues discussed in this paper are based on these neuropsychological findings.

Etiology of CNS Impairment

Numerous proposals as to the etiological basis of alcoholism-associated CNS impairment have been advanced. More than one of the etiological factors listed below may be involved in determining the CNS capability of any one patient. First, brain dysfunction may be a predisposing factor, rather than a consequence of alcoholism (Goodwin and Hill 1975). Tarter et al. (1977) found that adults who had exhibited signs of minimal brain dysfunction (MBD) as children were more likely to have a more severe form of alcoholism. Second, Victor and Adams (1961) indicated that malnourishment is a concomitant of alcoholism and concluded that CNS dysfunction in alcoholics results from deficient nutrition. Third, Kleinknecht and Goldstein (1972) and Goodwin and Hill (1975) noted that alcoholics frequently suffer repeated head injuries while drinking and suggested that these injuries could cause the reduced CNS capability. Fourth, liver disease (Rehstrom et al. 1977) and other medical complications related to the abuse of alcohol are known to produce brain dysfunction. Fifth, ethanol or one of its metabolically-related products can directly affect brain function. This view is supported by observations that alcohol consumption has obvious acute effects on CNS functioning and has been demonstrated to have direct chronic effects on other organ systems (Freund 1973).

Eckardt et al. (1978) examined some of these proposed etiological determinants but were unable to demonstrate a relationship between neuropsychological performance and prior or current physical or mental health condition, history of blackouts, seizures, or delerium tremens. Similarly, no relationship to cognition was

Table 1. Neuropsychological Performance of 116 Drug-Free Male Alcoholics, 2-31 Days From Their Last Drink

Test	Mean
TPT-dominant hand	7.7 min
TPT-nondominant hand	6.8[a] min
TPT-both hands	4.4[a] min
TPT-total time	18.9[a] min
TPT-memory	7.0
TPT-location	2.8[a]
Tapping, dominant hand	44.6[a]
Tapping, nondominant hand	40.8[a]
Trails A	39.5[a] sec
Trails B	98.2[a] sec
Categories	-74.1[a]
Speech perception	50.6[a]
Seashore rhythm	24.3[a]
Wisconsin Card Sorting Test	4.4[a] completed sets
Digit symbol	41.9
Digit span	10.9
Block design	30.2
Object assembly	28.4
Rod and frame, left tilt	-1.9°
Rod and frame, right tilt	-1.2°
Benton Visual Retention Test	5.1[a]
Shipley-Hartford, verbal	28.6
Shipley-Hartford, abstract	9.6
Shipley-Hartford, conceptual quotient	80.5[a]

[a] Performance at a level associated with brain dysfunction, according to the descriptive reference sources in Eckardt et al. (1978). Negative score reflects number of errors; positive scores reflect number correct or time.

found when Eckardt et al. (1978) considered blood chemistry values at admission, recent use of medication, vitamins, or frequency of missing meals because of drinking. In contrast, nonlinear combinations of recent and chronic drinking variables predicted neuropsychological performance, thereby supporting the concept of a direct toxic effect of ethanol. Further analysis of these complex drinking relationships revealed that certain patterns of alcohol consumption may actually accelerate the decline of brain function (Eckardt et al. 1978).

Short-Term Improvement

Regardless of the etiological basis, it is clear that alcoholics have decreased brain capabilities. Therefore, the suggestion that alcoholism-associated CNS impairment may improve with abstinence is of considerable clinical importance. This CNS improvement has been temporally conceptualized and discussed as a short-term phenomenon occurring between 1 to 3 weeks of abstinence and as a longer-term phenomenon (Page and Linden 1974).

Neuropsychological performance has been found to improve between the first and second to third weeks of abstinence (Allen et al. 1971; Weingartner et al. 1971; Smith and Layden 1972; Page and Linden 1974; Goldman and Rosenbaum 1976). Unfortunately, many of these studies did not use clinically accepted tests or failed to evaluate a wide spectrum of neuropsychological functions. Furthermore, appropriate control groups were not included often, so reported improvement may actually be due to the patients' taking the same set of tests twice within a short time period.

Eckardt et al. (1979) demonstrated little or no short-term improvement in performance on 24 commonly used clinical neuropsychological tests after controlling for repeated testing. In contrast, several other investigators have also controlled for practice effects, used commonly available cognitive tests, and reported improved performance (Jonsson et al. 1962; Page and Linden 1974). Between-group baseline differences in age, education, and cognitive performance might explain the purported improvement reported by Page and Linden (1974). The finding by Jonsson et al. (1962) that improvement occurred between the time when there was no alcohol in the blood or when hallucinations and delusions had subsided and approximately 28 days later suggests that short-term improvement may actually reflect initially decreased cognitive performance associated with withdrawal. Thus, short-term improvement in cognition may be complete when the clinical symptoms accompanying acute withdrawal have dissipated.

Long-Term Improvement

The possibility of improvement in cognitive performance with long-term abstinence is important because the demonstration of such a phenomenon would undoubtedly influence the planning of appropriate rehabilitation strategies, improve the adjustment to those aspects of life functioning that require relatively intact cognitive processes, and might motivate the patient to remain sober.

Long-term improvement has been claimed on the basis of electroencephalography (Bennett 1960), computerized tomography (Carlen et al. 1978), and neuropsychological studies (Long and McLachlan 1974; McLachlan and Levinson 1974; Ornstein 1977). The conclusions based on computerized tomography by Carlen et al. (1978) have been disputed (Hill and Mikhael 1979), and a number of investigators (Page and Linden 1974; O'Leary et al. 1977; Page and Schaub 1977) have been unable to demonstrate cognitive improvement with long-term abstinence. Some of the disparate results obtained with neuropsychological testing probably arise from the fact that the cognitive functions that can recover from long-term alcohol abuse do so at differing rates and are dependent, in part, on initial level of impairment, age, and sensitivity of neuropsychological tests. More long-term studies are required to determine if improvement in brain function accompanies prolonged abstinence.

Clinical Consequences of Alcoholism-Associated CNS Dysfunction

The finding of reduced CNS functioning in as many as 50 to 60 percent of the alcoholics entering treatment programs has prompted concern as to the prognostic significance of this impairment (Berglund et al. 1977; Parsons 1977; Eckardt et al. 1978). Therapeutic activities that would be of limited value if patients' cognitive functioning were compromised include intellectually-oriented forms of psychotherapy, occupational rehabilitation, and educational counseling on the adverse medical, psychological, and socioeconomic consequences of alcohol abuse. Concern over this issue has resulted in some alcohol treatment programs' already altering their therapeutic approaches in an attempt to increase treatment efficacy in cognitively impaired alcoholics (Caster 1977).

Even though a direct relationship between neuropsychological performance during treatment and subsequent outcome seems plausible, few investigators have specifically studied this question; those that have have reported different findings. Goldstein (1970) reported that treatment outcome did not differ between cognitively impaired and unimpaired alcoholics; McLachlan and Levinson (1974) observed no differences in cognitive performance among alcoholics who were subsequently abstinent and those who continued drinking. In contrast, Shelby and Goldstein (1976) suggested that normal performance on cognitive tests by employed alcoholics of relatively high socioeconomic status was associated with treatment success. Gregson and Taylor (1977) concluded that cognitive dysfunction had a dominant role in predicting treatment outcome, with poorer performance associated with relapse. Berglund et al. (1977) noted that those alcoholics who improved their drinking behavior performed better on psychometric tests administered during treatment. These discrepant results can be explained, in part, by the use of different neuropsychological tests and of different measures of treatment outcome.

Although some researchers have suggested (Allen et al. 1971; Weingartner et al. 1971; Page and Linden 1974) that those therapeutic approaches that require normal cognitive functioning should not begin until 2 to 3 weeks after cessation of drinking (so that the purported short-term improvement can occur), Eckardt et al. (1979) concluded that treatment can be initiated as soon as the clinical symptoms associated with acute withdrawal (ataxia, diaphoresis, extreme tremulousness) have subsided. Waiting an additional 17 days after detoxification did not measurably increase neuropsychological performance. Two apparent advantages of initiating treatment as soon as possible are to positively reinforce the patient's desire to seek treatment and to decrease the total expenditure of time and cost by the treatment facility.

A number of investigators (Armor et al. 1976; Pattison et al. 1977) have reported that some posttreatment alcoholics are able to resume drinking at moderate levels without apparent adverse effects and consequently have indicated that controlled drinking might therefore be an appropriate goal for certain alcoholic patients. Within the context of this paper, a critical question needs to be answered before accepting controlled drinking as an appropriate treatment goal: Are there any adverse neuropsychological consequences resulting from continued alcohol consumption?

In that linear and nonlinear combinations of drinking variables significantly predicted neuropsychological performances in alcoholics at the beginning of treatment (Eckardt et al. 1978), a similar analysis was conducted for performances determined approximately 7 months after completing treatment. This was accomplished by using the BMDP9R—all possible subsets regression program, with best defined in terms of minimizing the standardized total mean squared error of estimation (Hocking 1976). Age, education level, test score on the second administration (which occurred at the end of treatment), and posttreatment frequency of alcohol consumption and quantity (ounces of 100 percent ethanol) per occasion were included in quadratic multiple regression analyses as 5 first-order, 5 squared, and 10 first-order interaction terms. The resulting equations for 43 people with consistently reported and verified posttreatment drinking information are shown in table 2. These derived best equations significantly predicted performance for all 24 tests; the amount of variance explained (R2) was extremely large, indicating that the set of explanatory variables was robust.

Posttreatment consumption variables of frequency of drinking and quantity per occasion were observed either singly or jointly, to be explanatory variables in all but four cognitive tests. Examination of the remaining 20 equations revealed that they were composed of nonlinear and linear combination of variables, and drinking behavior was significantly related to posttreatment cognitive performance in a complex manner. Even though the mean values for posttreatment alcohol consumption were significantly decreased from pretreatment levels ($p < 0.0001$) both in number of drinking occasions (75 v. 320) and in quantity of 100-percent ethanol per occasion (3.3 v. 7.8 ounces), cognitive performance was still related to drinking behavior. These data indicate that the resumption of drinking by former alcoholics affects brain function, but the clinical consequences of this finding remain to be determined.

Table 2. Variables Included in Best Regression Equations Derived From 43 Former Alcoholic Patients

Test	Equation Variables	Overall p	R^2
TPT, dominant hand	$\overset{0.001}{(\text{T2 score})^{2}}:\overset{0.001}{(\text{T2 score}\cdot\text{qnt})}:\overset{0.003}{(\text{qnt}\cdot\text{ed})}:\overset{0.08}{(\text{qnt}\cdot\text{age})}$	0.0001	0.56
TPT, nondominant hand	$\overset{0.001}{(\text{T2 score})}:\overset{0.001}{(\text{T2 score}\cdot\text{frq})}:\overset{0.001}{(\text{frq}\cdot\text{ed})}:\overset{0.002}{(\text{T2 score})^{2}}:\overset{0.02}{(\text{qnt}\cdot\text{ed})}:\overset{0.08}{(\text{frq}\cdot\text{qnt})}:\overset{0.12}{(\text{qnt})^{2}}$	0.0001	0.83
TPT, both hands	$\overset{0.001}{(\text{frq})}:\overset{0.001}{(\text{T2 score}\cdot\text{frq})}:\overset{0.001}{(\text{frq}\cdot\text{age})}:\overset{0.007}{(\text{T2 score}\cdot\text{age})}:\overset{0.01}{(\text{frq}\cdot\text{qnt})}$	0.0001	0.72
TPT, total time	$\overset{0.001}{(\text{T2 score})}:\overset{0.001}{(\text{frq})}:\overset{0.001}{(\text{T2 score}\cdot\text{frq})}:\overset{0.005}{(\text{qnt})^{2}}:\overset{0.03}{(\text{qnt}\cdot\text{ed})}:\overset{0.06}{(\text{qnt}\cdot\text{age})}$	0.0001	0.81
TPT, memory	$\overset{0.001}{(\text{T2 score})}:\overset{0.001}{(\text{frq}\cdot\text{ed})}:\overset{0.002}{(\text{frq}\cdot\text{qnt})}:\overset{0.003}{(\text{T2 score})^{2}}:\overset{0.02}{(\text{qnt}\cdot\text{ed})}:\overset{0.04}{(\text{qnt})^{2}}:\overset{0.05}{(\text{age})^{2}}$	0.0001	0.57
TPT, Location	$\overset{0.001}{(\text{T2 score})}:\overset{0.002}{(\text{age})^{2}}:\overset{0.002}{(\text{ed})^{2}}:\overset{0.002}{(\text{age}\cdot\text{ed})}:\overset{0.008}{(\text{frq}\cdot\text{qnt})}:\overset{0.04}{(\text{frq})^{2}}$	0.0001	0.64
Tapping, dominant hand	$\overset{0.001}{(\text{T2 score})}:\overset{0.001}{(\text{T2 score}\cdot\text{age})}:\overset{0.002}{(\text{age})^{2}}:\overset{0.003}{(\text{qnt})}:\overset{0.01}{(\text{qnt})^{2}}$	0.0001	0.60
Tapping, nondominant hand	$\overset{0.001}{(\text{T2 score}\cdot\text{ed})}:\overset{0.001}{(\text{age}\cdot\text{ed})}:\overset{0.003}{(\text{frq})}:\overset{0.05}{(\text{T2 score}\cdot\text{frq})}:\overset{0.09}{(\text{frq})^{2}}$	0.0001	0.56
Trails A	$\overset{0.003}{(\text{T2 score})}:\overset{0.003}{(\text{qnt}\cdot\text{ed})}:\overset{0.007}{(\text{qnt})^{2}}:\overset{0.12}{(\text{qnt}\cdot\text{age})}$	0.0001	0.53

Table 2. Variables Included in Best Regression Equations Derived From 43 Former Alcoholic Patients (Con't)

Test	Equation Variables	Overall p	R^2
Trails B	0.001 0.001 0.001 0.001 0.001 0.001 (frq·qnt):(frq·age):(frq·ed):(qnt·ed):(T2 score·frq):(T2 score·qnt): 0.002 0.01 0.04 (T2 score)^2: (T2 score·ed):(ed)	0.0001	0.61
Categories	0.001 0.02 0.08 0.08 (T2 score):(qnt·age):(T2 score·qnt):(T2 score)^2	0.0001	0.69
Speech perception	0.001 0.002 (T2 score):(T2 score)^2	0.0001	0.72
Seashore rhythm	0.001 (T2 score)	0.0001	0.51
Wisconsin Card Sorting	0.001 0.006 0.03 0.05 0.06 0.12 (T2 score):(ed)^2:(T2 score·ed):(qnt)^2:(frq·age):(T2 score·age)	0.0001	0.59
Digit Symbol	0.001 0.001 0.01 (T2 score)^2:(qnt·age):(qnt)^2	0.0001	0.66
Digit span	0.001 0.001 0.01 (ed):(T2 score·ed):(ed)^2	0.0001	0.49
Block design	0.001 0.001 0.004 0.02 0.02 (frq):(T2 score)^2:(frq)^2:(qnt·age):(qnt)	0.0001	0.55

Table 2. Variables Included in Best Regression Equations Derived From 43 Former Alcoholic Patients (Con't)

Test	Equation Variables	Overall p	R^2
Object assembly	0.001 0.001 0.002 0.005 0.005 (T2 score):(T2 score·age):(qnt·ed):$(\text{qnt})^2$:(age·ed)	0.0001	0.62
Rod and frame, left tilt	0.001 0.001 0.002 0.006 0.02 0.02 (frq):(frq·qnt):(T2 score):$(\text{T2 score})^2$:(T2 score·frq):(age)	0.002	0.42
Rod and frame, right tilt	0.005 0.03 $(\text{qnt})^2$:(qnt)	0.005	0.24
Benton Visual Retention	0.001 0.005 0.007 0.01 0.02 0.04 (T2 score·ed):$(\text{qnt})^2$:$(\text{frq})^2$:$(\text{ed})^2$:(frq·age):(qnt·ed)	0.0001	0.59
Shipley-Hartford, verbal	0.001 $(\text{T2 score})^2$	0.0001	0.75
Shipley-Hartford, abstract	0.001 0.001 0.001 0.001 0.001 0.007 0.009 0.10 $(\text{ed})^2$:(T2 score·ed):(frq·qnt):(T2 score·frq):(frq age):(frq):$(\text{frq})^2$:(qnt·ed)	0.0001	0.84
Shipley-Hartford, conceptual quotient	0.001 0.001 0.003 0.005 0.02 0.02 0.10 (age):(T2 score·age):(T2 score·frq):(frq):$(\text{age})^2$:(frq·qnt):(frq·ed)	0.0001	0.78

Patients had consistently reported and verified posttreatment alcohol consumption. T2 score = score obtained on second test administration; ed = educational level; frq = posttreatment number of drinking episodes; an qnt = quantity of 100 percent ethanol consumed per drinking occasion. Probability levels are indicated above each variable.

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THE SWEAT-PATCH TEST: DEVELOPMENT OF A NEW METHOD TO MEASURE ALCOHOL CONSUMPTION

Michael Phillips

The Problem

No single test in current clinical use reliably tells a physician how much alcohol a patient is drinking. Consequently, alcoholism is often difficult to diagnose in its early stages, when patients may tend to understate their intake, and when there is no obvious evidence of tissue damage. In addition, there is no reliable way to monitor the effects of treatment for alcoholism to determine if patients are drinking any less.

There are many analogous situations in the history of medicine. One might imagine the quandary of a 19th-century physician caring for anemic patients without knowing their hemoglobin levels or hematocrits. The correct diagnosis was probably made only in the most severe cases, and then only late in the disease. A multitude of therapies abounded for anemia but, in the absence of a dependable measurement of outcome, it was difficult to determine whether iron pills were any more efficacious than arsenic, prayer, or sunshine.

As 20th-century physicians caring for alcoholics, we are faced with very similar problems when we attempt to assess how much alcohol a patient is drinking. Patients' self-reports of alcohol consumption are unreliable; many individuals can neither remember how much they have drunk, nor feel compelled to tell the truth about their recollections (Armor et al. 1978).

Neither are biochemical tests such as serum glutamate oxaloacetate transaminase (SGOT) and gamma-glutamyl transpeptidase (GGTP) of much use to the clinician. First, the tests lack sensitivity: They do not rise in response to alcohol ingestion except when large amounts have been consumed for long periods. Second, they lack specificity: Other factors, besides alcohol drinking, cause them to rise beyond normal limits (Jones 1979).

This lack of a dependable test for alcohol consumption has two major consequences: First, the diagnosis of alcoholism is frequently made late in the natural history of the disease, and only after severe organic or social damage has occurred. Second, the outcome of therapy cannot be well monitored.

Since the etiology of alcoholism is not well understood, treatments are inevitably empirical. Energetic enthusiasts propound a wide variety of therapies, including aversive drugs, Alcoholics Anonymous, psychotherapy, and poetry reading (Mazza 1979). Since outcome is so difficult to measure, we do not yet know with certainty which of these treatments is beneficial, harmful, or worthless.

The Hypothesis

Ethyl alcohol is readily measured in body fluids such as blood and urine. However, the information yielded by a single measurement of the ethanol level in blood or urine is very limited; one might make some tentative inferences about the amount of alcohol consumed in the preceding hours, but nothing can be said about the amount consumed over the preceding days or weeks.

Ideally, one might sample blood continually, around the clock for several days, and monitor the changing concentrations in blood ethanol. This procedure would provide detailed information about drinking behavior—the time the alcohol was consumed and in what quantity. However, in patients leading a normal life in the "real world" outside a hospital research laboratory, it is plainly out of the question to collect blood or urine continuously and reliably for several days or weeks at a time.

But what about other body fluids such as sweat? More than 100 years ago, Anstie (1874) demonstrated that alcohol is excreted in the sweat, and this observation has been confirmed many times (Brusilow and Gordes 1966; Pawan and Grice 1968). My former colleagues at the University of California at San Francisco, Ruth Vandervoort and Charles Becker, and I speculated that if sweat could be collected continuously at a steady rate, then the concentration of ethanol in the collected specimen should vary with the average concentration of ethanol in the blood during the period of the collection. This hypothesis, in turn, offered a totally new approach to monitoring alcohol drinking behavior over long periods.

At the outset, it was apparent that testing this hypothesis involved two distinct phases:

1. To develop a technique for collecting sweat continuously for several days (no method existed at the time) and
2. Having developed this technique, to evaluate it in alcohol drinkers.

Development of the Sweat-Collecting Patch

The first problem in a sweat-collecting device is to induce an area of skin to sweat continuously at a steady rate for several days. The second problem is to devise an adequate collecting system. It must be completely portable and hermetically sealed so that other fluids, such as bathwater, cannot contaminate the specimen, nor can the collected sweat be lost through evaporation or leakage.

We initially approached the problem of stimulating sweating for long periods by applying parasympathomimetic drugs such as pilocarpine to the surface of the skin under an occlusive dressing. This method was a complete failure.

An alternative approach was suggested by a study of British Air Force pilots, which attempted to determine their fluid losses during long periods of immersion in water (Brebner and Kerslake 1964). The researchers found that immersion in freshwater rapidly inhibited sweating (wet skin does not sweat). However, they found an interesting exception to this rule when they increased the salt content of the water.

This finding led us to suspect that fluid might cross the skin following an osmotic gradient. We tested this hypothesis using small pads of cellulose-based absorptive material (cut from Pampers diapers), impregnated with sodium chloride. These pads were applied to the skin under plastic adhesive tape, removed every day for weighing, then reapplied to the same location. We were gratified to observe a linear gain in weight over a 7-day period. In control pads with no added salt, the gain in weight leveled off after 2 or 3 days (Phillips et al. 1977).

These findings can be explained on the assumption that sweat dissolves the salt in the pad, generating a saturated hyperosmolar solution that bathes the skin and generates an osmotic gradient favoring the continued flow of fluid outward, across the skin. The salt is present in excess, so the solution is always saturated; hence the osmolarity of the solution and the osmotic gradient across the skin remain constant for several days.

We tested this hypothesis by substituting the sodium chloride with other soluble crystalloids (urea, fructose, magnesium sulfate), and obtained similar results in every case.

An improved version of the sweat-collecting patch is shown in figure 1. This device is easily and rapidly applied to the skin and is well tolerated by patients. This patch was evaluated in volunteers (Phillips 1980) and found to have linear uptake characteristics for periods up to 10 days (figure 2). When the patch is removed, the collected sweat is readily extracted by centrifugation.

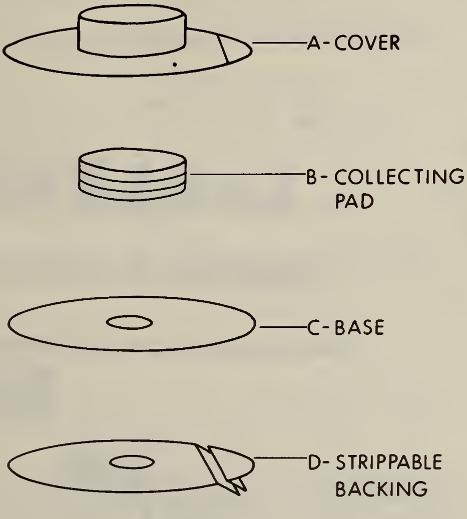
Testing the Sweat-Collecting Patch in Alcohol Drinkers

Having developed a usable sweat-collecting device, the next step was to test it in subjects consuming alcohol. In a pilot study of drinking volunteers, we found that ethanol was indeed present in the collected sweat, and that its concentration varied with two factors:

1. The average amount of ethanol consumed each day, and
2. The average concentration of ethanol in the blood during the period the patch was worn (Phillips et al. 1978).

These results confirmed that the measurement of ethanol in sweat offered a promising new approach to measuring alcohol consumption, but did not answer a number of important questions. Our pilot study had included volunteers drinking fairly continuously for 1 week. Would it still provide usable results in those drinking only intermittently? Furthermore, what was the lowest level of

Figure 1. "Exploded View" of Adhesive Collecting Patch

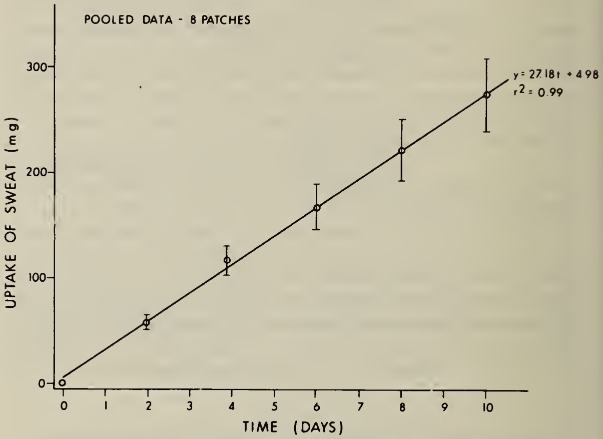


EXPLODED VIEW OF ADHESIVE COLLECTING PATCH

Base (B) and cover (A) are made of plastic surgical adhesive tape. Cover (A) may be plastic-backed at center and edge to facilitate removal of collecting pad. Strippable plastic backing (D) is removed immediately before applying patch to skin. Reprinted with permission, from *Biomater Med Devices and Artif Organs*, 8:13-21, 1980. Copyright 1980 by Marcel Dekker, Inc.

sensitivity at which drinking could be detected? And how specific was the test: Was there any overlap in the results obtained from drinkers and abstainers? All of these questions needed to be answered before the test could be used in clinical practice.

Figure 2. Uptake of Sweat by Collecting Patch Over a 10-Day Period

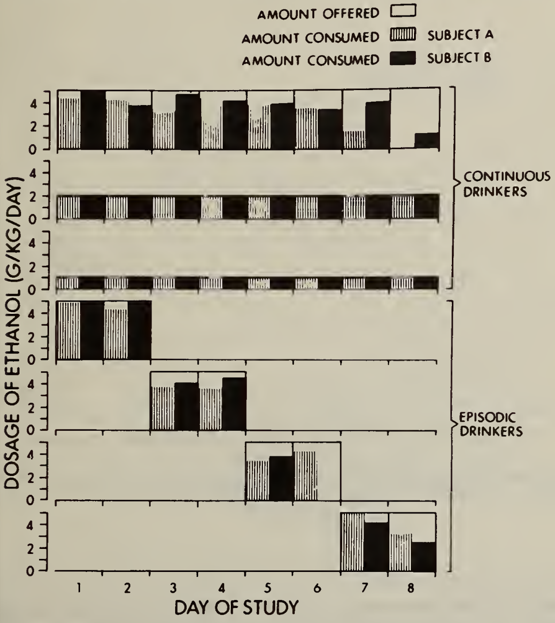


Bars show standard error of mean (SEM) of weight of sweat collected. Patches were weighed at approximately the same time; the SEM at time of collection is too small to be shown in this figure. Reprinted with permission, from *Biomater Med Devices and Artif Organs*, 8:13-21, 1980. Copyright 1980 by Marcel Dekker, Inc.

Figure 3 summarizes a study designed to answer these questions; it simulated patterns of continuous and episodic alcohol drinking in alcoholic volunteers (Phillips and McAloon, in press). We studied seven groups of two patients over an 8-day period. Three of the groups drank continuously for 8 days, but were offered different quantities: 1.0, 2.0, or 5.0 g ethanol/kg/d. The four remaining groups were offered 5.0 g ethanol/kg/d only during a 2-day "binge" and abstained the remaining 6 days.

At the outset of the study, 16 patches were affixed to the skin—8 on each leg. Four patches were removed every second day, and the sweat extracted and assayed for ethanol. Blood was sampled every 2 hours. The results are summarized in figures 4 and 5. Figure 4 confirms a finding of the pilot study, that there is a linear

Figure 3. Quantity of Alcohol Offered and Consumed



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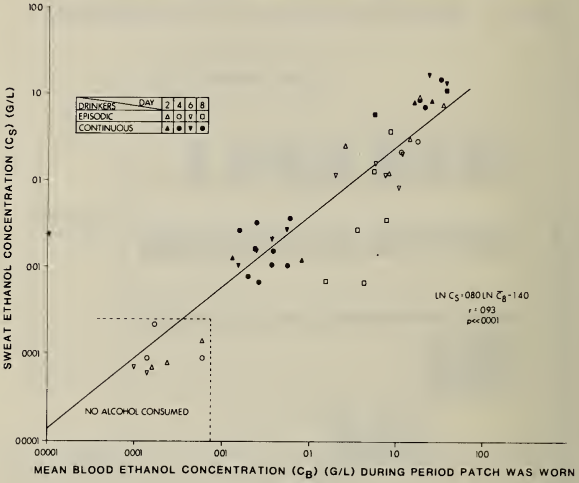
relationship between the sweat-ethanol concentration and the mean concentration of ethanol in the blood during the period the patch was worn. Results from continuous and episodic drinkers

Figure 4. The Variation of the Sweat-Ethanol Concentration with the Mean Concentration of Ethanol in the Blood During the Sweat Collection Period



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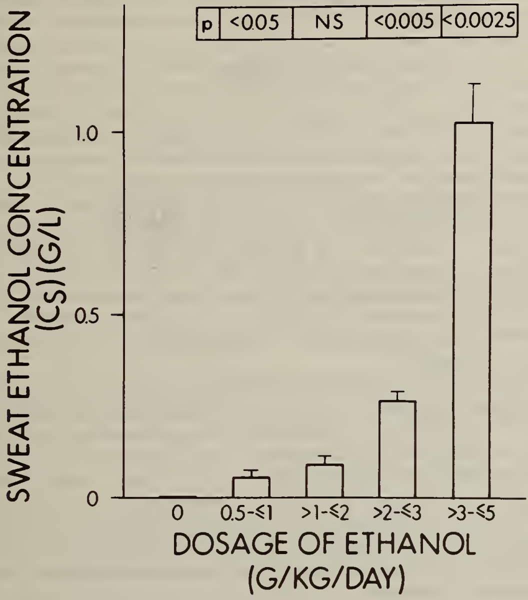
clustered about the same straight line. Figure 5 confirms another finding of the pilot study—that the sweat-ethanol concentration rises as more alcohol is consumed.

The test was sensitive enough to clearly distinguish nondrinkers from those consuming 0.5 g ethanol/kg/d, with no overlap of results from the two groups. This finding translates into 35 g ethanol/d in a 70 kg man, which is roughly the amount of alcohol in 3 fluid ounces of 100-proof spirits.

Figure 5. The Variation of the Sweat-Ethanol Concentration with the Dosage of Ethanol



This figure incorporates the values observed in continuous and episodic drinkers on days 2, 4, 6, and 8 of the study. Each bar shows the mean sweat-ethanol concentration observed in a particular dosage range, plus SEM. The values observed in each dosage range were compared to those of the next lower dosage range (p determined by single tailed t test). Reprinted with permission, from *Alcoholism:Clinical and Experimental Research* 4(4):1980. Copyright 1980 by Grune and Stratton.

Conclusions

The sweat-patch test appears to provide an objective index of alcohol drinking behavior in both continuous and episodic drinkers. It is both sensitive to and specific for alcohol drinking, and appears to be well tolerated by patients. However, before advocating the use of this test in a clinical setting, some notes of caution must be sounded: First, these studies have been performed mainly in hospitalized volunteers, drinking under highly controlled conditions. We do not yet know with certainly that the sweat-patch test will work as well in "free-range" drinkers outside a hospital.

Second, will patients agree to wear these patches? They will know that their level of drinking, formerly a subject of denial and debate, will now be exposed in a manner that brooks no argument. Obviously, a great deal depends on the relationship between the patient and the physician. My own experience has been that patients will cooperate with the test, provided it is presented in a nonthreatening manner, and they are assured the results will remain confidential.

Third, will it be possible for the patient to tamper with the patch and falsify the result? This problem is not as great as it appears: The patch will not adhere well to the skin again after it has been removed, so any tampering should be obvious. Also, the patches should be applied at least two at a time, and the two samples should closely correspond in sweat volume and ethanol concentration. In addition, the pad can be "spiked" with a dye that changes color on contact with air (reduced methylene blue, for example); the change would provide an immediate visual indication of leakage. Nonetheless, alcoholics are famed for their ingenuity, and it is not possible to guarantee that this method will remain completely tamper-proof in the future.

Fourth, could the act of wearing the sweat-patch influence patients to drink more or less alcohol than they might have drunk otherwise? This is a classic problem in the philosophy of science: the presence of an observer influencing the outcome of an experiment. My own guess is that patients might well alter their drinking habits when wearing the sweat patches for the first time, but this inhibiting (or encouraging) effect would wear off after a few weeks. Plainly this question requires further investigation.

Despite these potential problems, it is clear that the sweat-patch test provides a new approach to measuring drinking behavior.

Further studies are needed to evaluate the test in an outpatient setting, but it seems reasonable to expect that this test has potential applications in research and clinical practice.

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DISCUSSION OF PAPERS BY SCHEIG, LIEBER, ECKARDT, AND PHILLIPS

James E. O'Brien

I would like to make a few comments on the papers presented in this session: they not only point out the medical consequences of alcoholism, but also pinpoint several areas where there is dire need for immediate investigation. Foremost among these is the need for an objective measurement of the intensity of drinking. What we really need to know is not only what the consequences of alcohol abuse or intake are, but also at what levels these adverse effects occur, and what the predisposing factors are that render certain people more susceptible to cirrhosis or neurological complications.

Self-reporting of alcohol intake is remarkably unreliable. The present criteria used to establish the diagnosis of alcoholism leave much to be desired. In fact, we do not have any reliable means of determining the recent alcohol intake of any given individual. The present controversies regarding the significance of biological markers and the interpretation of results obtained in different laboratories under what are believed to be the same conditions will continue to persist until we can define objective measurements of intensity of drinking or what dosage of drug actually was administered. It is relatively easy to measure the various chemicals involved, yet it is very difficult to interpret their significance when one is not even able to define within reasonable limits the intensity and duration of recent alcohol intake.

The patch developed by Dr. Phillips shows remarkable promise, particularly when used in motivated individuals who are willing to use it and to follow directions. This test would be most helpful in epidemiological studies. We may be able to tell whether mail carriers drink more than police officers; whether full professors, because of money or desire, drink more than assistant professors. However, I am not quite sure what utility it will have for the hard-drinking individual on the street who is not well motivated, who is denying alcoholism, and who is unwilling to use the patch in the desired manner. We may be able to tell if it has been removed but, pharmacologically, we still will not have a measurement of the intensity of drinking in these individuals. For these people, the need for the biological markers remains.

Today, we hear much discussion concerning the appropriateness or the feasibility of what is referred to as "controlled drinking." Most often, discussions of controlled drinking center on the quantity of alcohol one can consume before being considered at risk from the alcohol. Unfortunately, this type of "limit-setting" completely ignores the marked variation in the susceptibility of different individuals to a number of serious adverse effects of alcohol. Despite years of research, we are still unable to determine which individuals who consume large quantities of alcohol will develop cirrhosis, which ones will exhibit central nervous system abnormalities, or who will exhibit marked effects on the eye, heart, or muscle. As Dr. Eckardt has pointed out in his studies with minimal brain dysfunction, there may be marked variations between individuals and their susceptibility to certain aspects of any given disease. Consideration of these variations in susceptibility to adverse effects readily points out that the setting of limits on the basis of the volume of alcohol consumed in and of itself will not be sufficient. Prudence indicates that we must postpone the concept of controlled drinking until such time as we are able, with a reasonable degree of reliability, to assure an individual that an alcohol intake below a specific quantity, at least for that individual, presents minimal probability of serious adverse effects.

I would also like to make some comments regarding the development of various levels of tolerance in individuals taking part in any biological study. All too often, studies on the effects of alcohol in humans or animals completely ignore the profound effects that tolerance may have on outcome. Many times, otherwise well-defined experiments lead to erroneous conclusions because tolerance is ignored. The administration of a given quantity of alcohol to an individual with a moderately high degree of tolerance may, in actuality, produce little if any physiological, pharmacological, or psychological effect. Therefore, one cannot rely on dosage alone as an indicator of the pharmacological action of alcohol but must, in all situations, determine and take into account the effects of tolerance in each of the patients on the overall response produced. Failure to account for tolerance can lead, and in many instances has led, to erroneous conclusions that alcohol may not produce specific effects on an individual or groups of patients.

Finally, the "revised" adage, that to know alcoholism is to know medicine, is undoubtedly true; unfortunately, the converse—to know medicine is to know alcoholism—is not necessarily true. All too often, the signs, symptoms, and consequences of alcoholism are treated as specific disease entities, and the constellation of signs and symptoms pointing out alcoholism as the underlying disease entity is completely ignored. It is hard for me to understand why curriculum committees devote so much time and grant substantial time to uncommon diseases rarely seen in medical practice and, at the same time, significantly limit or allow just minimal time to a disease that very conservatively affects at least 14 percent of our patients.

I think the papers presented here again point out the necessity of allowing sufficient time in the medical school curriculum to give adequate instruction in the recognition and treatment of alcoholism. However, an allotment of time sufficient to deal only with the medical aspects of alcoholism will bring little change in the care of these patients unless we also devote sufficient time to dealing with the various attitudes of health professionals to treating this extremely prevalent and unfortunately chronic disease.

SESSION VI: ASSESSMENT OF TREATMENT IMPACT

THE RAND REPORTS: RECONCILING RESEARCH AND TREATMENT PERSPECTIVES*

David J. Armor

When the Rand report *Alcoholism and Treatment* (Armor et al. 1976, 1978) was released, it was met with unprecedented public controversy concerning its finding that some alcoholics return to normal drinking after treatment. Although normal or controlled drinking by alcoholics has been the subject of scientific disagreement for at least a decade, never before had the issue been debated so intensely in the public arena. The controversy did much to reveal a rift between certain research and treatment perspectives about the nature of alcoholism and its proper treatment, and especially the issue of abstention versus drinking goals for alcoholics. The origins and significance of this conflict are described most fully in an *American Journal of Psychiatry* article that appeared, ironically, just 1 month following publication of the first Rand report (Kalb and Propper 1976).

Disagreement between research and treatment professionals on treatment methods is clearly unusual in the health fields. No doubt, it reflects inadequacies peculiar to alcoholism in both scientific and clinical observation. The credibility of research is often marred by methodological problems, and clinical opinion is frequently shaped by emotional involvement of observers who themselves are recovering alcoholics, with heavy personal stakes in the outcome of the debate. No doubt the Rand controversy reflected both of these influences.

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* This work was supported, in part, by contract #ADM281-76-0006, from the National Institute on Alcohol Abuse and Alcoholism. Views expressed in this paper are the author's own and are not necessarily shared by Rand or its research sponsors.

Whatever the reasons, it is clear that, given our responsibilities to the victims of alcoholism, a gap between the findings of research and the practice of treatment is indefensible. Both the researcher and the clinician have the common objective of helping alcoholics overcome the devastating effects of the disorder. This goal can be accomplished only by mutual respect for each group's unique experience and insight, whether it be the everyday experience of the lay person, the clinical observation of the practitioner, or the systematic investigation of the scientist. We must pull out the kernel of truth in each seemingly conflicting perspective, thereby providing a firmer foundation for the treatment of alcoholism.

The purpose of this paper is to discuss how the Rand reports relate to the disagreement regarding treatment goals for alcoholics. It is contended that, although the Rand research helped fuel the debate, it also has produced a set of findings that may ultimately contribute to a resolution of the conflict. The paper begins with a brief review of the first Rand report, focusing on what it said (and did not say) about normal drinking. This review is followed by a summary of the findings of the second Rand report regarding the drinking versus abstention issue (Polich et al. 1980). These empirical results set the stage for a discussion of the origins of the abstention-drinking debate, and the way in which the Rand research may help reconcile existing research and treatment perspectives.

The First Rand Report

The controversial finding of the first Rand report actually had two parts. First, it was reported that a substantial portion of a large, national sample of alcoholics treated at National Institute on Alcohol Abuse and Alcoholism (NIAAA) centers were engaging in what was defined as "normal" drinking at an 18-month followup. Normal drinking was one of three types of remission patterns distinguished by the study; the other two were longer term abstention of 6 months or more, and short-term abstention lasting anywhere from 1 to 5 months before the followup interview. Normal drinkers were persons who drank less than 3 ounces of ethanol per day in the past month, and who had no frequent alcohol dependence symptoms or behavior impairment. Drinkers in the past month who drank more than this limit, or who had frequent problems, were classified as nonremissions. According to this definition, about one-fourth of the national sample were long-term abstainers, one-fifth were short-term abstainers, one-fifth were normal drinkers, and one-third were nonremissions at the 18-month followup. In effect, nearly as many alcoholics were engaging in normal drinking as were abstaining for fairly long periods.

This pattern of improvement among treated alcoholics is not at all unusual in the research literature (Emrick 1974; Baekeland et al. 1975). Indeed, had the term "improvement" been used in the Rand report, the level of discord might have been significantly reduced. Unlike scores of other studies, however, that term was abandoned in favor of "normal" drinking. In retrospect, this choice of terminology had unintended consequences that bred confusion among the general public and hostility among treatment professionals. The term "normal" was intended to mean levels of alcohol consumption and impairment corresponding to statistical variations observed in general populations; in other words, the "norm" in ordinary society. But Blume (1977) may have been correct, in a critique of the Rand report, when she said that to treatment people, "normal" drinking conjures up an image of spontaneous, joyful problem-free drinking," a picture not justified by the data. Apart from statistical qualities, it is quite likely that moderate or controlled drinking by alcoholics differs in quality and style from that of the average social drinker. Whatever the differences may be, the substantive issues involved here are too complex and too important to get lost in a semantic battle. The second Rand report drops the term "normal" drinking, in favor of the more neutral term of "nonproblem" drinking.

Aside from the terminological problem, the finding of a group of moderately drinking alcoholics (at one point in time) is itself a contradiction of what we might call the classical "loss-of-control" theory of alcoholism. According to this conception, the true alcoholic will lose control over drinking after only one or two drinks so that, at a given time, alcoholics will either be abstaining or drinking in an uncontrolled alcoholic fashion. Needless to say, this extreme conception is clearly inconsistent with virtually every followup study of treated alcoholic samples, including the first Rand report (Lloyd and Salzberg 1975; Pattison 1976). Although there may be some alcoholics who fit this pattern, it is fair to say that few experienced and sophisticated treatment professionals subscribe to this oversimplified version of the loss-of-control theory.

The second and even more controversial finding about normal drinking in the first Rand report had to do with relapse. The origin of what we call a "relapse" analysis is itself revealing about some of the more sophisticated theoretical perspectives in the alcoholism field. When early drafts of the Rand report were being reviewed, several treatment professionals criticized inclusion of normal drinking as a form of remission, on the grounds of what might be called a revised abstention theory. This conception follows formulations by Keller (1972) and Ludwig and Wikler (1974), and might be stated as follows: When alcoholics begin drinking again after a period of abstention, many frequently pass through a stage of controlled, moderate drinking. However, this stage can be maintained only temporarily, and total relapse becomes highly likely if not inevitable. In other words, loss of control after resumption of drinking is not necessarily instantaneous, but may take a matter of weeks or months. Given that the 18-month followup interview used a 30-day window to assess detailed drinking behaviors, this revised theory predicts that at any given time some alcoholics might be found who appear to be moderate drinkers, but who in truth are simply advancing toward total relapse. If such is the case, then moderate drinkers should not be counted as remissions on the basis of a single followup.

The relapse analyses were designed to investigate this dynamic view of alcoholic remission and relapse. If the revised abstention theory is correct, then normal drinkers identified at one followup should have a high rate of relapse by the time of a second followup; abstainers, especially long-term abstainers, should show a lower rate of relapse. To test this hypothesis, a subsample of the study cohort was classified into various remission statuses according to a 6-month followup, and their subsequent statuses were determined as of the 18-month followup. A relapse would be a person in remission at the 6-month followup, who was a nonremission at the 18-month followup. Contrary to the predictions from the revised abstention theory, no significant differences were found in the relapse rates for long-term abstainers (17 percent), short-term abstainers (19 percent), or normal drinkers (13 percent). Moreover, very few of the normal drinkers became long-term abstainers at 18 months; many more remained in normal drinking status. Ironically, therefore, the case for classifying normal drinking as a form of remission was strengthened, rather than weakened, by the longitudinal analysis suggested by the revised abstention theory.

Needless to say, critics were quick to point out the methodological weaknesses of the NIAAA data used in the first Rand study. The sample used for the relapse analysis was small (200 cases); drinking behaviors were based solely on self-reports; the followup response rate was only 62 percent; followup interval was not that long (18 months); and the window of observation for drinking behavior was narrow (30 days). Being acutely aware of these same problems, the report concluded that the findings should not be the basis of policy until they could be tested with stronger data. It also pointed out that only *some* alcoholics adopted normal drinking, and that the data at hand could not distinguish those who could safely return to normal drinking from those who could not. Moreover, it was observed on a priori grounds that some alcoholics, such as those with liver damage or those with a history of repeated failures at maintaining moderate drinking, could not safely return to moderate drinking. Unfortunately, these cautions and qualifications were ignored by some of our critics who claimed the Rand report advocated controlled drinking policies for all alcoholics.

The Second Rand Report

The second Rand report is based on a 4-year followup study of the same cohort studied at 18 months (Polich et al. 1980). Given the controversy about the first report, the design of the 4-year study gave high priority to solving some of the methodological limitations of the 18-month followup. The 4-year followup has a much larger set of variables for assessing alcoholic impairment, including mortality; it has longer 6-month and 4-year windows within which to evaluate drinking behavior; it has two independent studies of the validity of self-reports; and it has a respectable response rate of 85 percent of the *original* cohort samples for the 18-month study. This high response rate yielded a large sample of about 500 male subjects, whose relapse patterns could be studied over a much longer period—between 18 months and 4 years after treatment.

The 4-year study includes methodological investigations whose results are interesting in their own right. The special validity studies did uncover some underreporting, but not enough to seriously affect the results. Using both collateral interviews and blood alcohol concentrations (BACs) determined from breath tests, it was found that self-reports of abstention, major drinking-related events, symptoms of alcohol dependence, and amount of consumption (among recent drinkers) were reasonably accurate. Although amount of consumption was underreported to some extent, when this underreporting is taken into account in the most conservative sensitivity test, the results are not altered to a significant degree.

This is not to say that the 18-month and 4-year studies have identical results. The expanded set of measures over a wider 6-month window at 4 years led to a tightened definition of remission. First, when short-term abstainers last drank, they tended to have very severe problems. Second, existence of only a few symptoms of alcohol dependence (tremors, blackouts, morning drinking) was associated with other serious problems, even among lighter drinkers; heavy consumption itself did not portend significant problems in the absence of dependence symptoms. Therefore, the definition of remission at 4 years eliminated short-term abstention, and counts even a few symptoms of dependence as evidence of continued problem drinking.

The final definition of status at 4 years thus distinguishes between three major groups, based on behavior in the past 6 months: long-term abstainers for 6 months or more; nonproblem drinkers; and problem drinkers who show signs of alcohol dependence or serious adverse consequences (in areas of health, job, interpersonal relations, for instance) in the past 6 months. The first two categories are treated as remissions. Given this new definition, the second Rand study reports a remission rate of 46 percent at the 4-year followup, compared with 67 percent at 18 months. Remissions include 28 percent who are longer term abstainers, and 18 percent who are classified as nonproblem drinkers.

Most important, the broader data base of the 4-year followup study made it possible to conduct a more comprehensive analysis of relapse, focusing on the period between 18 months and 4 years. The new relapse analysis benefits not only from a longer period of observation, but also from the use of multiple relapse criteria. The criteria represent different definitions of relapse between the 18-month and 4-year followups. A relapse can be defined as (1) a person experiencing problem drinking at the 4-year followup, based on the new 6-month window; (2) a person experiencing any problem drinking between the 18-month and 4-year followups; or (3) a person alive at 18 months who died of alcohol-related causes by the time of the 4-year followup.

The results for these three different criteria of relapse are summarized in table 1. First, the new status definition at 4 years, based on a 6-month window, shows that long-term abstainers at 18 months have the lowest rate of relapse (30 percent), but this figure is not significantly lower than the 41-percent relapse rate for nonproblem drinkers. Short-term abstainers have a relapse rate of 53 percent, highest of the three improved groups at 18 months. The second row shows the rate of any problem drinking between 18 months and 4 years; again the pattern is similar. As expected, the larger window raises the overall level of relapse for all groups. Nonetheless, both long-term abstainers and nonproblem drinkers have significantly lower relapse rates than the short-term abstainers—whose problem rate nearly equals that for 18-month problem drinkers. The longer term abstainers have a slightly (but not significantly) lower rate than nonproblem drinkers. Finally, the percentage of alcohol-related mortality is low for long-term abstainers and nonproblem drinkers, but relatively high for the other two groups.

It appears, then, that the second Rand study offers little support for a revised abstention theory, at least for one holding that abstention yields a substantially better prognosis for all alcoholics taken as a group. Although the relapse rate of long-term abstainers is slightly lower than that of problem drinkers, the difference is not large enough to confer a distinct disadvantage on nonproblem drinkers. Clearly, many longer term abstainers relapse, and many nonproblem drinkers do not.

The result raises the important question of whether the relapse rates for abstainers and nonproblem drinkers are uniform throughout the sample. Do all subgroups in the study have about the same prognosis for nonproblem drinking as for abstention? In other words, is it possible that some persons can adopt nonproblem drinking (or abstention) without much chance of relapse, and others cannot? In the 18-month study, no characteristics differentiated normal drinkers who relapsed from those who did not. The 4-year study, however, has different results. In effect, it found that the prognosis of abstention versus nonproblem drinking depended on the alcoholic's age, level of alcohol dependence, and marital status at the time of admission to treatment.

The differential relapse rates are shown in table 2. This relapse analysis uses a 30-day window at 4 years, so overall relapse rates are somewhat lower than shown in table 1. The rates are percentage of relapses, estimated from a logit regression in which the interaction of 18-month status with age, level of alcohol dependence, and marital status at admission all have significant coefficients. The interactions present a complex pattern of relapse, depending on one's drinking status at 18 months and one's group membership at admission. For older persons with high levels of dependence at admission, long-term abstention at 18 months had a better prognosis (7 percent relapse) than did nonproblem drinking (39 percent relapse). But the situation reverses for younger men with lower dependence, in which case nonproblem drinking yields a better prognosis (5 percent relapse) than long-term abstention (24 percent relapse).

Table 1. Relapse Patterns at 4 Years

	Status at 18 Months			
Status at 4 years	Abstained 6 months or more	Abstained 1-5 months	Nonproblem drinking	Problem drinking
Percent problem drinking in past 6 months	30%	53%	41	73
Percent problem drinking between 18 months and 4 years	45	70	55	84
(N)	(115)	(99)	(85)	(175)
Percent alcohol-related death between 18 months and 4 years	1.4	8.9	2.9	9.0
(N)	(140)	(124)	(103)	(223)

For older men with low dependence or younger men with high dependence at admission, marital status plays the deciding role: Married men do better with long-term abstention (9 percent relapse) than with nonproblem drinking (22 percent relapse);

unmarried men do better with nonproblem drinking (10 percent relapse) than with abstention (19 percent relapse).

Table 2. Estimated Percent Relapsing at 4 Years by Characteristics at Admission[a]

Characteristics at admission	Status at 18 Months Abstained 6 months or more	Nonproblem drinking
High level of dependence, age 40 and over[b]	7	39
Low level of dependence, age under 40	24	5
High dependence, under 40 or low dependence, over 40:		
Married	9	22
Unmarried	19	10

[a] Rates estimated from a logit regression model in which age, dependence level, and marital status had significant interaction coefficients with status at 18 months. (See Polich, et al., 1980, for details).

[b] Low dependence in 1 to 10 episodes of alcohol dependence symptoms (blackouts, tremor, morning drinking) during the 30 days before admission.

These new relapse results do not support the revised abstention theory, but they do lay a foundation for yet another theory of relapse: The efficacy of abstention and the risks of nonproblem drinking are not constant for all alcoholics but, rather, vary from one person to another depending on the individual's characteristics and environment at the time treatment starts.

Existing theories of alcoholism do not readily explain these interactions, especially the high rate of relapse for long-term abstainers who are younger, less dependent, or unmarried. Younger, unmarried men are less likely to be in social environments that are supportive of abstention, at least compared to those of older married men, so the variables of age and marital status may well be surrogates for environmental conditions. As the Alcoholics Anonymous (AA) experience has taught us, supportive environments are critical for changing such deeply engrained behaviors as alcohol dependence; without support, or in hostile environments, the stress of change may be too heavy for a problem drinker to carry alone. Younger, unmarried persons may be more likely to find support for moderated drinking; older, married men may find support for abstention but hostility for attempts at moderate drinking, especially from their wives.

The finding for low versus high levels of alcohol dependence suggests the possibility of a threshold in the degree of alcohol dependence, beyond which the ability to return to nonproblem drinking is substantially reduced. In this respect, the findings of the second Rand report converge with some recent work on dependence by Edwards and his colleagues (1976). After a certain level of dependence is attained, physiological changes may occur that make it very difficult for the alcoholic to return to moderate drinking.

Whatever the reasons for these interactions, the existence of differential relapse rates for abstainers versus nonproblem drinkers, if verified and replicated in other studies, could have important implications for future treatment policies. They may also provide a basis for reconciling different views on the drinking-abstention issue.

Closing the Research-Treatment Gap

Does the Rand research offer any insights for understanding and perhaps helping to bridge the gulf between research and treatment perspectives? How can the research findings on nonproblem drinking be reconciled with the abstention theory dominant among treatment professionals? First, the type of evidence on which the abstention theory is based must be considered. For example, Jellinek's original studies of alcoholism gave abstention-only theories their most important scientific boost, but those data were based on retrospective case studies of Alcoholics Anonymous members, most of whom had attained successful, long-term abstention (Jellinek 1946, 1952). In effect, Jellinek's samples were largely self-selected groups who had certain histories in common. Most important, they had all found that long-term abstention was the best solution for their drinking problems. This conclusion may be valid for the group in question, but the problem here is one of generalization from a self-selected subgroup to the population of all alcoholics. The samples were mostly long-term abstainers, not a cross-section of all alcoholics; thus, a generalization that abstention is the only workable solution for all alcoholics is clearly unwarranted.

Similar problems of generalization may arise from the experience of treatment practitioners. Given the emphasis on abstention, the only cases likely to be seen by the average clinician are successful abstainers, some of whom will maintain contact with the clinic, and relapses, who require further treatment. Those who return to drinking without serious problems may not have the same probability of exposure to clinics as the other two groups. This situation may lead clinicians to underestimate the true proportion of nonproblem drinkers in the alcoholic population at large.

Prospective followup studies like Rand's are gradually building up a picture of the natural history of alcoholism on samples that are more complete and are followed over longer periods than most clinical observations. At any one time, longer term abstainers make up only a fraction of the Rand samples, and the continuous abstainers over the entire 4 years comprise an even smaller group (only 7 percent). According to attitudinal measures, most longer term abstainers resemble Alcoholics Anonymous members in their belief that they cannot return to "controlled" or social drinking without eventual serious relapse, including death.

But there is also a group—albeit smaller than the longer term abstainers—that is drinking without problem at followup. Just as the abstainers did, most of the nonproblem drinkers did not maintain this status throughout the entire 4-year period. But unlike the abstainers, the Rand study shows they have not accepted the belief that alcoholics cannot drink, and they do not believe serious harm will befall them if they continue to drink. Clearly, this group would not be discovered by conducting retrospective studies of AA members.

The foregoing observations help explain the research-treatment gap, but what about closing it? The second Rand report and its findings about differential relapse, if replicated, may offer a pathway to ending the dispute about abstention versus drinking for alcoholics. In defense of classical theories of alcoholism, there does appear to be a large subgroup for whom moderate drinking substantially increases the risk of relapse compared to abstention. The classical theory could be modified to incorporate the abstention-only edict only for persons who are *severely* dependent (rather than merely dependent or nondependent) and who are older or married. To the extent that current treatment practices advocate abstention for these persons, there would be no disagreement with Rand's current research.

On the other hand, the Rand research finds other alcoholic subgroups for whom abstention yields a worse prognosis than nonproblem drinking, a finding not reflected in current treatment practices. Particular attention might be drawn to the younger, unmarried alcoholic, for whom nonproblem drinking yields lower relapse rates than absention, regardless of dependence level. Is it possible that the single-minded emphasis on abstention for all alcoholics, without regard to background or environmental characteristics, might be hampering (rather than promoting) remission from alcoholism?

The second Rand report, like the first, does not advocate a change in abstention policy at this time. Nonetheless, this research opens the door to a new perspective on alcoholism. If the Rand findings hold up in future research, a different, more complex picture of alcoholism and its treatment may be needed. Rather than a monolithic group to be treated with the single goal of abstention, alcoholics may be a heterogeneous group, demanding differential diagnoses (especially for level of dependence) and differential treatment goals. Such a theory of alcoholism would not only help reconcile the conflicting perspective on alcoholism among researchers and treatment professionals; it might also ultimately increase remission rates from this chronic, relapsing illness.

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DIFFERENT STROKES FOR DIFFERENT FOLKS: DIFFERENTIAL TREATMENT FOR ALCOHOL ABUSE

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Clinicians, for some time, have adapted their therapeutic approach to suit the specific needs of each client. This common practice, termed "eclectic" or "individualized" therapy, is generally accepted as good clinical care. Thus, it may seem odd that researchers have been hard-pressed to demonstrate the efficacy of differential treatment, that is, the matching of clients to specific interventions. Indeed, alcoholism researchers have encountered enough problems showing the efficacy of any treatment above that of minimal intervention or placebo or of a spontaneous recovery.

This paper examines factors that underlie this apparent discrepancy. In particular, it is argued that previous research has failed to identify client type by treatment interactions because many studies did not possess the technical feasibility of finding such effects (if, indeed, they do exist). First, the basic requirements for a technically feasible test of client-treatment matching are outlined. Then, preliminary evidence from the alcoholism treatment literature is reviewed to support the matching of client types with specific interventions. Although some interesting trends are suggested, the data are far from conclusive. Finally, the search for client type by treatment interactions in other domains is examined. Research on the treatment of depression is especially enlightening.

The Basic Question

"Different strokes for different folks" implies the tailoring of treatment services to meet the particular needs of a given client. This tailoring is based on the premise that not *all* alcohol abuse clients can benefit from *all* treatment modalities; different types of clients respond better to different types of treatment. Although the matching of treatment and client has received considerable attention in the recent literature (Beutler 1979; Ewing 1977; Mandell 1975; Pattison et al. 1977; Wanberg et al. 1977), this need was pointed out almost 40 years ago by Bowman and Jellinek (1941). Furthermore, some 20 years ago Wallerstein (1957) provided evidence that certain client types responded better in alternative treatment programs.

From the outset, one must recognize that considerable channeling of clients to treatments already exists. Obviously, a client with acute liver pathology is not recommended to a controlled drinking program, an unmarried client is not referred to marital counseling, and someone with a history of cardiac problems or suicidal tendencies is not prescribed disulfiram. The central question, then, is to establish the *degree* of specificity, justified by empirical research, in matching clients with treatment.

Outside of a few specialized treatment centers for alcoholism, most health care settings offer only one program for alcohol abuse. This program is generally a multimodal treatment package (Glaser 1977), consisting of medical care, group or individual counseling, educational lectures, and recreational activities. In a procrustean fashion, clients are encouraged to participate in all aspects of the program.

Research Design Requirements

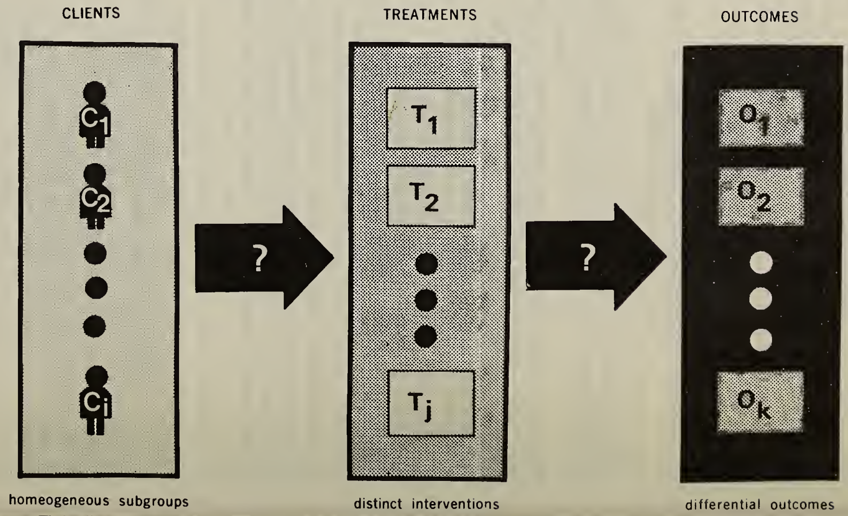
A prototype of an alcoholism treatment system is shown in figure 1. This multivariate model, adapted from Pattison et al. (1969), distinguishes among three classes of variables. First, among *client variables*, the essential question is whether or not one can identify relatively homogeneous subgroups with unique syndromes of alcohol-related problems. In short, are all "alcoholics" more or less the same, or are meaningful subpopulations present? Second, with respect to *treatment variables*, the central issue is the degree to which interventions are sufficiently distinct and well defined. Although alcoholism treatment programs may have different names, in actual practice they often use the same basic approach. Third, to what extent are *treatment outcomes* multidimensional? Is there evidence for differential outcomes from treatment, or does a global unimproved-improved continuum exist?

1. Equal Representation of Client Types in Alternative Treatment Modalities

The rationale for requiring equal representation of client types is straightforward. Because of admittance criteria and self-selection by clients, a given treatment program generally deals with a restricted sample. How would one know whether a specific client type would improve in a program if that group is always underrepresented? A recent study by Finney and Moos (1979) provides an excellent illustration of this issue. Alcoholic clients from five residential treatment programs were empirically clustered into four high and four low social competence groups. However, client types were *not* systematically distributed across the five programs. Low social competence types were more frequent in the Salvation Army, public hospital, and halfway house programs; high social competence types predominated in the milieu-oriented and aversion conditioning programs. Certain client types rarely participated in some particular programs (few low social competence patients in milieu therapy, for instance), so one has scant data on how these clients would have fared if treated with this method. (This underrepresentation problem was acknowledged by the authors.) Thus, it is not at all surprising that their intensive search for client type-program interactions yielded no significant results.

There is growing evidence that one can identify distinct subgroups among alcohol abuse clients, and that many of these types are similar to clients found in a general psychiatric population (Skinner 1979; Skinner et al. 1974, 1976). Earlier research focused on the delineation of clinical syndromes, such as the "essential" versus "reactive" types proposed by Knight (1937) and elaborated by Rudie and McGaughran (1961). Recently, there has been a proliferation of empirical typologies identified through the use of cluster analytic techniques. Although limitations have been noted in this body of research (Morey and Blashfield 1979), one point is clear: The population of alcohol abusers is multivariant (Pattison

Figure 1. A Prototype Model of an Alcoholism Treatment System



Multivariate Treatment Model

et al. 1977). Treatment research that does not consider these more homogeneous client subgroups runs the risk of "averaging out" important treatment effects (Goldberg 1972).

2. Distinct, Well-Defined, and Controlled Treatments

Over time, treatments must be distinct, well-defined, and controlled. Although two interventions can be given different names and expound different principles, in practice they may overlap considerably. Most treatments are offered in a social context, and there usually is ample opportunity for common elements to appear, such as interactions with fellow clients or casual conversations with staff members. Also, the procedures and quality of a given intervention may "drift" over time. Initial enthusiasm and cohesiveness by staff members introducing a new therapeutic approach may wane and methods revert to those used before.

Again, the study of Finney and Moos (1979) illustrates these problems. Although five treatment programs were examined, each offered a variety of services and there was considerable overlap between services at each setting. For example, most offered Alcoholics Anonymous (AA) meetings and some type of group therapy. One must seriously question whether these programs were sufficiently distinct to enable the emergence of client type-by-program interactions.

The large-scale study by Smart (1978) has similar limitations. Four types of treatment were evaluated: (1) "mainly" individual; (2) "mainly" group; (3) equal combinations of group and individual; and (4) individual only. Even though 1,091 alcoholics were studied, the great majority of clients (83.4 percent) received only individual treatment. Furthermore, there was considerable heterogeneity among the professions of the principal therapists—physicians, 46.7 percent; social workers, 30.1 percent; pastoral counselors, 0.2 percent—and profession varied according to the geographic location of the clinic (Gillies 1972). Thus, the Smart (1978) study is predominantly an analysis of one "loosely defined treatment."

3. Multiple Outcome Measures

To demonstrate differential treatment outcomes, multiple variables must be included in the study. For example, a client's alcohol consumption may decrease and the level of depression be exacerbated, or vice versa. There has been a growing emphasis on the multidimensional assessment of treatment outcome, and on community followup at several points in time (Lowe and Thomas 1976). Standardized instruments have been developed, such as the Followup Adjustment Questionnaire (Foster et al. 1972), which accounts for various factors including abstinence, controlled drinking, employment-productivity, sociopathy, intrapersonal adjustment, and social involvement.

In a recent study, Hart and Stueland (1979) found that different types of alcoholics yielded different rehabilitation outcomes. Three months after discharge from treatment, five subgroups achieved varying levels of success as determined by seven measures of rehabilitation status (economic security, physiological problems, family relationships, for instance). Nevertheless, the five subgroups failed to be differentiated on measures of drinking status. This study is a good example of the need to assess multiple rehabilitation criteria; an emphasis on drinking status alone would have concealed differential rehabilitation in other life areas.

4. Adequate Statistical Power

Given that the above requirements have been met, a particular analysis must also have adequate statistical power to detect real treatment effects (Cohen 1969). Otherwise, there is a clear danger of being "deceived" by the empirical data. In brief, "statistical power" refers to the probability of detecting a significant treatment effect (that is, reject the null hypothesis) when indeed a real effect exists in the population. Unless one has a reasonable chance of empirically demonstrating the existence of a treatment effect (say, a 90-percent chance), one must seriously question whether the time and expense involved in conducting the study are justified.

Consider a study to evaluate the utility of a measure (social stability, for instance) in predicting successful outcome at 1-year followup. Research has found social stability to be a consistent predictor of outcome (Ogborne 1978). Assume that the "true" predictive validity of the social stability measure is 0.35. Under ideal conditions—the reliability of the followup criterion is perfect and all clients entered the treatment program (no preselection)—a sample size of 82 clients is needed to have a 90-percent chance of empirically demonstrating a statistically significant relationship. With more realistic conditions of criterion reliability (for example, a reliability coefficient of 0.70) and 50 percent of the client pool preselected for the program, adequate statistical power (90-percent chance of detection) would be attained only with a sample of *314 clients*! As Schmidt et al. (1976) concluded, "sample sizes required to produce adequate power in empirical validation studies are substantially larger than has typically been assumed."

The danger is that, because of insufficient statistical power, one may be misled by the empirical data: That is, one may conclude falsely that a particular treatment program either does not work or does not generalize to different treatment settings. In truth, the treatment program may be reasonably successful "in the population." Because of different levels of statistical power across studies, however, varying levels of success in detecting treatment effectiveness can be achieved. Schmidt and Hunter (1977) provided an ingenious demonstration of this issue in their study of validity outcomes across similar jobs in personnel settings. Although wide variation was observed in validation results from study to study, they accounted for this distribution by a Bayesian model that considered differences only in sample sizes, selection ratios, predictor reliability, and criterion reliability. The model assumed an identical underlying validity coefficient in each study.

The parameters of sample size, selection ratio (preselection of clients), predictor reliability, and criterion reliability vary from study to study (Baekeland 1977), and these factors alone may account for the inconsistent and inconclusive results in the search for prognostic indicators of alcoholism treatment outcome. How many treatment studies had adequate statistical power to demonstrate a significant effect in the first place?

Evidence to Support Client-Treatment Matching

A general consensus from the alcoholism treatment literature is that client characteristics are more important with respect to outcome status than is the kind of treatment given. At the end of their exhaustive review, Baekeland et al. (1975) concluded that "over and over we were impressed with the dominant role the patient, as opposed to the kind of treatment used on him, played both in his persistence in treatment and in his eventual outcome." All forms of treatment seem to produce the same relative level of success (Armor et al. 1978; Baekeland et al. 1975; Edwards et al. 1977; Emerick 1975). Why is this so? Client-treatment matching, largely fueled by client self-selection of treatment programs, is one explanation for these uniform success rates (Blane 1977). Stated differently, client *mismatching* with treatments may dilute the overall success rate, and mask the presence of a better outcome status for certain client types in certain treatment programs.

There is considerable evidence, however, that does not support client type-by-treatment interactions, such as the Finney and Moos (1979) and Smart (1978) studies already described. Furthermore, the Rand study examined various client type/treatment type combinations and found none to be effective (Armor et al. 1978).

These three studies were *observational* rather than *experimental.* In contrast, the evidence to support client-treatment matching invariably comes from experimental studies that randomly assigned clients to treatment conditions. Table 1 summarizes studies that directly address the issue of client-treatment matching. In all cases where the experimental design involved random assignment, empirical evidence was found to support client-treatment matching. Perhaps as Annis (1979) suggested, the failure to discover evidence for matching is more a function of ineffective or inappropriate research design.

The Wallerstein (1957) and Kissin et al. (1970) studies are frequently cited to support the matching hypothesis, although methodological problems have been noted with each (Ogborne 1978). Wallerstein (1957) discerned some interesting interactions among psychiatric diagnoses and improvement rates among inpatients who were randomly assigned to (1) Antabuse therapy, (2) conditioned reflex therapy, (3) group hypnotherapy, and (4) control (milieu) therapy. However, clients in all four groups were in treatment at the same time and there were commonalities (such as group therapy) across all conditions. Also, differential success was achieved in gathering followup data across the four treatments, a factor that could have biased the results.

Kissin et al. (1970) compared four treatment conditions: (1) outpatient drug therapy; (2) outpatient psychotherapy; (3) inpatient rehabilitation; and (4) no therapy for 6 months. They concluded that "socially and psychologically stable patients do best in psychotherapy; the socially intact but psychologically less sophisticated patient does better under drug therapy; and the socially unstable but intellectually intact patient does best on an inpatient rehabilitation program." However, only 50 percent of the clients were located successfully at a 1-year followup, and contamination occurred in the randomization procedures such that the groups were not homogeneous on intake variables. Thus, the findings should be viewed as suggestive.

Table 1. Studies of Client-Treatment Matching

Study	Random assignment of clients to treatment	Evidence for matching
Wallerstein (1957)	Yes	Yes
Kissin, et al., and Su (1970)	Yes *	Yes
McLachlan (1972, 1974)	Quasi	Yes
Orford et al. (1976)	Yes	Yes
Glaser's (1979) reanalysis of Merry et al. (1976) and Reynolds et al. (1977)	Yes	Yes
Armor et al. (1976)	No	No
Smart (1978)	No	No
Finney and Moos (1979)	No	No

*Some contamination occurred.

McLachlan (1972, 1974) provided more convincing data, examining the match between conceptual level (CL) of the client and principal therapist. This dimension compares individuals who tend to be poorly socialized, egocentric, dependent, and cognitively simple (low CL), with individuals who are seen as independent, self-assertive, questioning, and cognitively complex (high CL). Accordingly, directive psychotherapy should be appropriate for low CL clients, and nondirective therapy should be more suitable for high CL clients. In this study, clients were assigned to one of five therapists on a rotational, quasi-random basis. Followup data (12 to 16 months) were collected on 94 of the 100 clients participating in the study. The results, summarized in table 2, revealed statistically significant interactions. The recovery rate of clients matched to therapists on CL was 70 percent, compared with 50 percent for the mismatches. Similarly, clients matched to therapists on aftercare exhibited a 71-percent recovery rate, compared with a 49-percent recovery for mismatches. Finally, clients matched to both therapist and aftercare achieved a 77-percent recovery rate. The recovery rate for mismatches to both therapists and aftercare was only 38 percent. These data suggest that, as the degree of refinement in client-therapist matching increases, concomitant improvements in treatment outcome accrue.

Table 2. Recovery Rate by Client–Therapist Match

	Clients matched	Clients mismatched
Therapist	70%	50%
After-Care	71%	49%
Both	77%	38%

Further support for client-treatment matching is evident in the 2-year followup data of the widely cited trial of "treatment" and "advice" by Edwards et al. (1977). In this study, 100 married male clients were randomly assigned to either a standard package of help (inpatient-outpatient) or a minimal intervention group that received one "advice" session. An inspection of the 2-year followup data revealed a client type-by-treatment interaction (Orford et al. 1976; Glaser 1979). That is, clients diagnosed as physically dependent or gamma alcoholics in Jellinek's system achieved better results in the treatment condition; other clients did better with the minimal intervention or advice condition. Furthermore, an interaction was found with drinking status at the 2-year followup. Abstainers were more likely to have been diagnosed as gamma alcoholics at intake, whereas controlled drinkers were more likely to have been diagnosed as alpha alcoholics. Although the sample sizes in these comparisons were small, the results are promising.

Finally, evidence for client-treatment matching has been given by Glaser (1979) in a secondary analysis of two earlier studies. Glaser examined data from a controlled trial of lithium carbonate versus a placebo condition, in which subjects were classified as depressed or nondepressed via an objective measure (Merry et al. 1976; Reynolds et al. 1977). Depressed clients showed a significant reduction in days spent drinking during lithium treatment. The nondepressed clients showed no difference in number of drinking days during lithium or placebo treatment.

Differential Show-Rates for Treatment

The following example reinforces the value of examining client-treatment subgroups. More specifically, this study (in which Hau Lei, Allen Zweben, and Bonnie Jeffery collaborated with the author) addresses the prediction of treatment dropouts. Stated positively, this means the prediction of which clients following an initial assessment will actually show up at the first appointment of their assigned treatment program. The sample includes 347 clients who voluntarily sought help for alcohol- or drug-related problems at the Clinical Institute of the Addiction Research Foundation, Toronto. Following a 2-day comprehensive assessment program, clients were assigned to one of three broad treatment categories:

1. Inpatient (N = 133): Multimodal treatment, offering a variety of services, such as group therapy, vocational rehabilitation, and relaxation training;
2. Outpatient (N = 135): Traditional modes of psychotherapy, such as individual and marital counseling; and
3. Basic care (N = 79): Brief sessions of supportive counseling and help with practical matters.

A variety of psychosocial assessment variables were examined as predictors of which clients would attend their first treatment appointment.

Tables 3 and 4 illustrate, quite dramatically, how an analysis of the total sample masks the presence of relationships for clients subgrouped according to treatment category. For example, the Social Role Maladaption scale from the Alcohol Use Inventory (Horn et al. 1974) does not predict show-rates for the total sample ($r = 0.03$); it might be concluded that this scale is not a useful predictor. However, an examination of client subgroups reveals that Social Role Maladaption has a significant *negative* correlation with inpatients (clients who are more socially adapted tend to show), a *near zero* correlation for outpatients, and a significant *positive* correlation with basic care. When the total sample is analyzed, these relationships cancel each other, and appear as a near zero correlation. A similar trend for marital status is revealed in table 4. In the total sample, married clients are significantly less likely to appear for treatment. Nevertheless, among inpatients *all* married clients appeared, in contrast to the trend exhibited by outpatients and clients in basic care. These data suggest that differential prediction models (Wiggins 1973) are needed for each treatment category.

Table 3. Correlation With Show-Rate at Treatment

	Total	Treatment Subgroups		
	N = 347	Inpatient N = 133	Outpatient N = 135	Basic Care N = 79
Social Role Maladaption (AUI)	.03	- .23**	.04	.24*

* p<.05

** p<.01

Search for Matching in Other Domains

In 1928, Hull noted that validity coefficients for predicting success in educational and personnel settings rarely surpassed 0.50. Some 40 years later, Ghiselli's (1966, 1973) exhaustive reviews confirmed this prediction ceiling. Ghiselli (1966) concluded that "the maximal power of tests to predict success in training is of the order of 0.50, and to predict success on the job itself is of the order of 0.35." Strategies have been proposed to raise these upper limits—to search for more homogeneous groups of individuals and the interaction of these subgroups within different training or employment contexts (Dunnette 1966). Such research has been subsumed under the heading moderator variables. Although some encouraging findings have been noted (in particular, to predict law school success of different student types, Klein et al. 1968), the search for moderator variables overall has produced limited results (Zedeck 1971).

Table 4. Show Rate at Treatment

	Married	Not Married
Total Sample N = 347	58%	75%
Treatment Subgroups		
Inpatient N = 133	100%	72%
Outpatient N = 135	49%	82%
Basic care N = 79	53%	77%
	$p < .05$	

Recently, Cronbach and Snow (1977) reviewed the educational literature on student aptitude by treatment interactions. The central question is whether different teaching methods are equally effective for different groups of students. Their review covered several hundred studies and discussed methodological problems in the analysis of interactions. In brief, Cronbach and Snow found some consistent interactions: (1) General intelligence interacts with instructional aids; (2) Prior experience interacts with method of instruction; and (3) Students high in constructive motivation perform better when teaching is less directive, and students high in defensive motivation perform better when there is less demand for self-direction. Although the authors concluded that interactions exist, they noted difficulties in finding replicated results. One must also remember the sheer magnitude of this literature when comparing it with the eight studies from the alcoholism treatment literature (table 1).

Of greater relevance to the alcoholism field are some promising studies regarding the relationship between empirically derived classifications of depression and response to chemotherapy. Blashfield and Morey (1979) reviewed 11 studies that used empirical clustering procedures to identify relatively homogeneous subgroups among clinically depressed patients and found a notable consistency. All studies identified a retarded-endogenous-psychotic type that contained the most severely depressed patients. Moreover several nonpsychotic types were found. Four studies identified a neurotic cluster; four found a hostile type; and six found an anxious depression subgroup. Of particular note is the finding that certain types responded best to different forms of chemotherapy (Hollister et al. 1967, 1971; Overall et al. 1966; Paykel 1972; Paykel et al. 1973; Prusoff and Paykel 1977; Raskin et al. 1972; Raskin 1974). A relatively consistent finding is that the retarded-endogenous-psychotic type responds best to tricyclic antidepressants; the anxious depression type is most successfully treated with the major and minor tranquilizers.

Of particular relevance is the finding that, in the treatment of anxious depressed psychiatric inpatients, patients with histories of alcohol abuse responded differently than did other patients. In two double-blind controlled experiments, Overall et al. (1973) found a significant interaction between alcohol history and drug treatment. A summary of their findings is given in table 5. Patients with a history of alcohol abuse responded best to treatment with phenothiazines; patients lacking a history of prior alcohol abuse were better treated with the benzodiazepine antianxiety drugs. Thus, the literature on the treatment of depression provides heartening support for the concept of matching client types with treatments. Moreover, it is noteworthy that these studies were experimental, not observational, and that they randomly assigned clients to treatment conditions.

Conclusion

Four basic requirements for a "technically feasible" study of client-treatment matching have been reviewed.

1. Client types must be equally represented in alternative treatment conditions. Experimental designs that randomly

assign clients to treatment are preferred to nonrandom assignment.

2. Treatment conditions must be distinct, well-defined, and controlled.
3. Multiple outcome measures must be employed at several stages of followup (end of treatment, 6 months, 1 year, 2 years). Outcome criteria must include important sociobehavioral-biomedical factors, in addition to drinking status.
4. Adequate statistical power is needed so the investigator has a reasonable chance of detecting treatment effects (if, indeed, they exist).

Table 5. Improvement Scores in Response to Drug Therapy

	Alcohol Abuse	
Drug Therapy	History	No History
Phenothiazines	13.8	6.9
Benzodiazepines	8.6	10.3

$p < .001$

These requirements are stringent but, unless they are met, the issues of client-treatment matching have not been fairly addressed.

Of the four basic requirements, most problematic is the development of treatment modalities that are sufficiently distinct and powerful. Many health care settings offer only one approach (Glaser et al. 1978) to alcoholism, and this package is often multimodal. Such a treatment regimen makes it nearly impossible to ascertain which components are most effective, superfluous, or even deleterious for different types of clients. Elsewhere, this approach has been termed a "smorgasbord of modalities" (Skinner 1979). From my experience, the temptation to overindulge at a smorgasbord is irresistible. However, afterwards one has great problems identifying which dishes were especially tasteful and which delicate morsels are presently causing indigestion.

Future research on client-treatment matching should consider three directions. First, there is no substitute for experimental studies that randomly assign clients to treatments. All studies that supported client-treatment matching in alcoholism treatment used an experimental (as opposed to observational) design (table 1). Moreover, the studies that found consistent client type-by-chemotherapy interactions to depression employed experimental designs. Second, more powerful interventions are needed at earlier stages for the treatment of alcoholism. New techniques are being developed, and as more powerful interventions are developed and systematically tested, client type-by-treatment interactions should proliferate.

Third, valuable leads can be generated by carefully studying the differential decisionmaking processes of experienced clinicians. This author is well versed in the literature on clinical judgment, is aware of Meehl's (1965) "box score" on clinical versus statistical prediction, and is cautioned by the experiments of Tversky and Kahneman (1974), among others, on the fallibility of human judgment. The evidence shows that clinicians are good at constructing decision models, but inconsistent in applying them. Thus, one should focus on creative ability in identifying *what* the key variables are and *how* they should be used to make treatment decisions (Wiggins 1973). Some clinicians are quite effective in treating alcohol-related problems, and their actions should be studied.

The fundamental issue centers around the *degree* of matching that is justified by clinical evidence. Clearly, in the treatment of alcoholism, the level of refinement in matching clients with treatments is at a fledgling stage. Nevertheless, the search for client-treatment interactions is vital for improving treatment effectiveness. For the clinician, it would facilitate the planning and delivery of treatment services with specific client subgroups. For the researcher, it would enhance understanding of the complex factors involved in the treatment process and lead to the development of more cogent theoretical models of alcohol abuse. For the administrator, it would guide the efficient allocation of scarce treatment resources.

In conclusion, if one is to have a fair test of client-treatment matching, treatment programs *must* be appreciably distinct; client types *must* be adequately represented in each program; and multiple outcome measures *must* be collected. All shortcuts are problematic.

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OUTCOME CRITERIA AND THE ASSESSMENT OF ALCOHOL TREATMENT EFFICACY

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Does treatment work? Superficially, this question seems easily answered. In practice, however, the definition and measurement of alcohol treatment outcomes have been fraught with methodological and conceptual problems (Hill and Blane 1967; Sobell 1978*a*,*b*; Voegtlin and Lemere 1942). Recently, though, there have been significant advances in methodological sophistication, especially in the areas of alcohol treatment outcome criteria and assessment. For example, global outcome measures have been replaced with more precise and quantifiable measures; new techniques have reduced the followup attrition rate; and multivariate assessment models have replaced drinking behavior as the sole yardstick of treatment efficacy. Although significant advances have occurred, major problems still exist, and various techniques and measures need further refinement. This paper discusses specific deficiencies and areas of refinement in the context of a proposed set of prototypical measures and procedures for evaluating alcohol treatment efficacy.

A Prototype for Assessing Alcohol Treatment Outcome

Standardization

A standardized method of measuring drinking behavior would have obvious value for assessing and comparing the effectiveness of different alcohol treatment approaches and programs. Presently, however, standardized procedures and measures do not exist to assess drinking behavior or other areas of life-health functioning (Maisto and McCollam 1980). Drinking behavior and other dimensions of treatment outcome (vocational function, residential status, for instance) have typically been defined and measured idiosyncratically within studies. It may be unreasonable to expect complete standardization of outcome assessment procedures and measures, but the establishment of some criteria for all alcohol treatment outcome studies is necessary to validly synthesize the findings of multiple outcome studies. In this way, common findings can be elucidated across investigations. Unfortunately, there is now such a serious lack of comparability among studies that only grouped results can be examined for gross similarities. Furthermore, it is difficult to compare the criteria used in individual studies, because investigators often describe their procedures and measures in vague or ambiguous terms.

At the least, all studies of alcohol treatment outcome should include a basic assessment of drinking behavior and associated areas of life-health functioning (e.g., physical health, vocational function), using measures that conform to the following psychometric characteristics: (1) operationally defined; (2) quantifiable, and continuous if possible; (3) reliable; and (4) valid. For example, rather than subjectively assessing ethanol consumption according to categories such as "abstinent," "improved," "no change," or "worse," researchers should obtain more precise data that specify a person's specific pattern of ethanol consumption in terms of amount consumed per day. It this way, even though arguments may persist as to what constitutes a safe or improved level of drinking, at least data could be compared for different studies.

Similarly, other measures of life-health functioning can and should be quantifiably and continuously defined. For example, the measure of vocational stability is considerably more continuous and exact when it is measured in number of days employed full-time and amount of earnings per month, than when it is seen in nominal categories of "improved," "same," or "worse." These more precise measures are also amenable to more sensitive statistical analysis.

Defining measures operationally not only increases measurement precision, but also decreases the chance of subjective bias' clouding the interpretation of outcome results. That is, disagreements may exist regarding what types of outcomes constitute risk, but at least the disaccord could be related to the interpretation of outcome data rather than to a lack of comparability among studies.

Another problem with using nominal categories to evaluate outcomes is that such measurement may be seriously biased by variable temporal reference points. For example, what is evaluated as improved one month may be evaluated as worse or unchanged on another occasion. Vague notions of whether a treatment program "works" are no longer satisfactory. Peer reviewers such as journal editors must enforce greater standards of scientific quality when accepting outcome studies for publication.

Most alcohol treatment outcome studies still present data in terms of grouped outcomes. In these cases, treatment "X" is superior to treatment "Y", but what therapeutic interventions produced what specific changes in specific clients under what conditions is unknown. To answer such specific questions, individual subject functioning before, during, and after treatment must be known. Individual subject change scores permit the evaluation of how treatment affected different areas of life-health functioning for different subjects. From such data hypotheses can be generated about the nature of effective treatment; these can then be subjected to empirical testing. Finally, and perhaps most important, by knowing what treatments are successful with what types of individuals, subjects can be better matched with treatments, rather than assigned on the basis of imprecise and unsubstantiated clinical judgment.

Planned Evaluations

The value of planned versus retrospective assessments is obvious. Planning, and especially pilot testing of, treatment outcome evaluation methods and measures can help resolve various problems. Planned studies also have an advantage in that researchers can inform subjects about the followup, request their continued and full compliance with that followup, and obtain necessary tracking information (addresses, phone numbers, collaterals). Planned evaluation studies are thus able to complete followup with a very high percentage of subjects (Ersner-Hershfield et al. 1979; Moos and Bliss 1978; Sobell and Sobell 1976). Given that several studies have shown that subjects lost to followup are typically functioning less well than those found (Barr et al. 1973; Moos and Bliss 1978; Sobell and Sobell 1978*a*), attrition must be minimized in order to draw valid and unbiased outcome conclusions.

Self-Reports

Another set of issues concerns sources of outcome data and the interpretation of outcome results. For years, the validity of alcohol abusers' self-reports has been questioned, on the grounds that the individuals lie or distort their reports to portray their functioning more positively than is actually the case. In the last few years, a concerted effort has been made to assess different aspects of the validity and reliability of different populations of alcohol abusers' self-reports (Cooper et al. 1979, in press; Maisto, Sobell, Cooper, and Sobell 1979; Sobell 1976; Sobell and Sobell 1975, 1978*b*; Sobell et al. 1974, 1979*a*, *b*). Collectively, these studies have shown that the self-reports of drinking and drinking-related behaviors (arrests, hospitalizations, accidents, probation) for different clinical populations of alcohol abusers are relatively reliable and valid when obtained in clinical treatment settings and when the subjects interviewed are alcohol-free. The one instance in which alcohol abusers' self-reports appear to be frequently invalid is when they are asked about their recent drinking behavior and they have some level of alcohol in their bloodstreams (Sobell et al. 1979*b*). When alcohol abusers have not been drinking and their self-reports are discrepant with other data sources, it is usually because the subjects have described themselves more negatively than either official records or their collaterals' reports. That is, subjects report more arrests than the records show and report more serious drinking problems and symptoms than their collaterals report (Guze et al. 1963; Maisto, Sobell, and Sobell 1979; McCrady et al. 1978).

Convergent Validity

The most important criterion that must be fulfilled by treatment outcome measures is that the results obtained must validly reflect behavior occurring in the natural environment. Any outcome measure or assessment technique must fulfill the scientific criteria of reliability and validity. To date, such basic requirements have scarcely been acknowledged, much less implemented. The efficacy of any treatment cannot be determined with measures whose reliability and validity have not been established.

No outcome measure, in isolation, has yet been shown to be error-free, and it has been suggested that investigators use a convergent validity approach to assess drinking and related behavior over extended followup periods (Sobell and Sobell 1979). Using this approach, the strength of a study's conclusions is based on the amount of convergence among multiple outcome indicators. Thus, assessment of treatment efficacy is based on data derived from as many sources as possible, including (1) subjects' self-reports; (2) multiple collateral informants' reports (friends, relatives, employers, probation officers, neighbors); (3) infield probe breath alcohol tests; (4) official records to verify reports of incarcerations, employment (paycheck stubs), driving infractions, disabilities, marriages, divorces, deaths; (5) periodic liver function tests to assess recent episodes of heavy drinking; and (6) any other measure of value to a specific study. "When a variety of relatively independent measures of outcome are employed and are mutually corroborative, evaluators can have confidence in the validity of their outcome conclusions" (Sobell and Sobell 1979). Another benefit that can accrue from the use of a convergent validity approach derives from identifying discrepancies among data sources. Resolving discrepancies can lend further confidence to outcome conclusions.

Multiple Populations of Alcohol Abusers

Another criterion that should be fulfilled by alcohol treatment outcome studies is a detailed specification of the population studied. Typically, studies in the alcohol field have presented outcome or assessment data for a single population of alcohol abusers. Consequently, these studies must include cautions that their results may not apply to other populations of alcohol abusers. Defining a study's subject population is critical to the interpretation of results as well as to the generalization of findings. This restriction is particularly important in that the majority of alcohol treatment programs have, until very recently, studied chronic or *gamma* alcoholics (Jellinek 1960). In the last few years, however, there has been an increasing emphasis on providing services for individuals with less serious alcohol problems. In addition, "study population" must include *all* clients who enter treatment—not just those who complete it.

Published reports of various alcohol assessments and treatment techniques using more than one population of alcohol abusers have reported differential findings for the various populations studied. Although limited in number, these studies have shown that different populations of alcohol abusers (1) exhibit different patterns of treatment outcome (Hart and Stueland 1979; Moos and Bliss 1978; Pattison et al. 1973; Schmidt et al. 1968); (2) require different followup strategies (Moos and Bliss 1978); (3) give slightly different degrees of reliable and valid self-reports (Cooper et al. 1979; Maisto, Sobell, Cooper, and Sobell 1979; Sobell and Sobell 1978*b*); and (4) may show different directions of invalidity when self-reports are invalid (Cooper et al. 1979). Thus, it may eventually be necessary to develop different assessment procedures for different subject populations.

Pretreatment Measures

The collection of comprehensive data regarding subjects' pretreatment functioning is important. Using a battery of pretreatment measures has three distinct advantages. First, a battery of measures can serve to clearly define the subject population and, as mentioned earlier, this definition is critical to the interpretation and generalization of a study's findings. Second, multiple pretreatment measures can be used to assess differential levels of pretreatment impairment. Some populations start treatment with very different levels of functioning than others, so multiple pretreatment measures can be used to control for basement and ceiling effects prior to treatment. Such data can be compared with posttreatment data to assess amounts of change during treatment for groups, as well as for individual subjects. Finally, regression analysis of pretreatment measures can evaluate those variables that relate to subjects' successful functioning. Such information can be used to assign subjects to different treatment modalities, based on empirical data rather than on clinical judgment.

Treatment Factors

In addition to satisfactory descriptions of the populations under study, it is equally important to specify the nature of the treatment delivered. At the present time, there are no consistently successful alcohol treatment approaches or programs. Thus, identifying, reporting, and preferably measuring all known treatment components are essential to knowing what variables might have contributed to a subject's improvement, lack of change, or deterioration. Some treatment factors, such as treatment type and length, and sex of therapist, can be readily identified and reported. However, other less specific treatment factors, such as rapport or motivation, should not be ignored, even though they might be more difficult to identify and define.

Nonspecific treatment factors will need to be discussed if their impact is to be assessed. Compliance with treatment, for example, can be defined in several ways: (1) the ratio of the number of treatment sessions attended to the number of sessions scheduled; (2) the ratio of the number of assignments completed outside of treatment sessions to the number of total assignments agreed on; (3) the ratio of the number of appointments canceled in advance to the total number of sessions missed; and (4) the ratio of the number of sessions attended on time to the number of total sessions attended. Considering the present state of the art in the treatment of alcohol problems, coupled with the recent challenges (Armor et al. 1978; Edwards et al. 1977; Emrick 1975) that treatment type makes no noticeable difference, it is clear that rigorously designed clinical research studies are needed. With appropriate definition and assessment, multivariate statistical techniques can play a valuable role in suggesting which treatment components are most related to positive outcomes.

Assessment Length Intervals

Assuming that subjects and treatments have been appropriately defined and a battery of adequate pretreatment measures determined, the next logical consideration is the necessary interval to use for gathering pre- and posttreatment data. Data have recently emerged suggesting that for chronic alcoholics a retrospective interval of 12 months is needed to evaluate pretreatment drinking behavior adequately. Cooper et al. (1979) found that a 30-day pretreatment interval is not representative of the drinking behavior of chronic alcoholics. This study also found that, for less chronic alcohol abusers, data representing a 30-day pretreatment interval differed little from data for longer pretreatment intervals. The above findings are relevant to the measure of daily drinking behavior and do not reflect the adequacy of pretreatment intervals for other types of life-health variables; so these authors suggest an interval of at least 12 months to assess all pretreatment variables.

The results of several studies in the past several years have helped to determine an adequate time interval during which posttreatment data must be gathered to reflect stable functioning. These findings indicate that after an interval of 18 months (reviewed in Sobell and Sobell 1978*a*), group data change very little. Prior to the 18-month interval, however, changes in group data are frequent. Although these data are for groups of subjects, data for individual subjects continue to show some variability even after 18 months.

A final issue regarding intervals involves the evaluation of outpatient alcohol treatment programs and when the followup interval should formally begin. Unlike the hospital setting (where treatment is usually completed within a specified time period and there is a precise discharge date), outpatient treatment has traditionally been more open-ended. Consequently, it is more difficult to determine a specific discharge date; the boundaries of formal treatment are not necessarily distinct or clearly demarcated. Another consideration with outpatients is that their treatment occurs while subjects live in their usual environments; thus, their functioning is not sheltered or restricted as compared to patients in hospital settings. Thus, for outpatients, followup should start when subjects first enter treatment. In this way, the followup data can also be used to determine what types of extratreatment factors interfere with treatment gains and, therefore, how treatment might be modified to counteract these factors.

Multiple Measures of Outcome

In terms of what kinds of outcome data should be gathered, a recent review (Maisto and McCollam 1979) of the alcohol treatment literature concluded that alcohol treatment studies that used multiple measures of life-health functioning to assess treatment efficacy showed tremendous variability in the types, number, definition, and quantification of the variables used. Obviously, consumption of alcohol is, without question, a necessary target behavior in assessing alcohol treatment efficacy, but most alcohol specialists agree that other areas of an alcohol abuser's life functioning are likely to be affected either by a person's drinking problems or as a result of treatment. Whether changes in other areas of life-health functioning are antecedent or consequent to drinking, the changes should be assessed, pre- and posttreatment. The relationships of posttreatment changes in drinking behavior need to be evaluated in the context of other possible changes in the patient's life. It is also important to know the temporal relationships between various aspects of treatment outcome. For example, do changes in drinking behavior precede or follow changes in interpersonal functioning, and do different types of subjects show different patterns of change?

Another reason to use measures other than drinking behavior to evaluate treatment efficacy is because a review of past studies (Maisto and McCollam 1979) has shown that drinking, in and of itself, is not always sufficient to give a clear picture of the subject's functioning. Some individuals who drink excessive amounts of ethanol show no immediate, related life-health dysfunction. But some abstinent alcoholics have not demonstrated improved functioning in other areas and, in fact, have even shown deterioration (Pattison 1978).

Some indexes of treatment outcome, although easily measured, are not easily interpreted as showing improvement or dysfunction. For example, to assess change in marital status, should divorces be considered good or bad outcomes? Does long-term continued attendance at Alcoholics Anonymous meetings after hospital discharge demonstrate successful functioning or a dependence on this group to maintain functioning? The answers to these questions are, of course, debatable and subject to different clinical interpretations. In these and similar instances, it is advantageous to collect and report complete data. Investigators may infer certain conclusions from their data; others reading the reports can evaluate whether they agree with those conclusions. Presenting the data on which conclusions are based isolates the data from their interpretation.

Multiple measures of life-health function have been included in many treatment outcome studies, and additional measures are needed. For instance, another way to assess drinking behavior outcomes is to measure subjects' preoccupation or cognitive fixation with alcohol. For example, people who regularly, and out of fear, structure their daily living (never going to a party, avoiding all places that sell alcohol) to avoid contact with alcohol might be considered to be preoccupied with their possible return to drinking. Similarly, people who repeatedly think of alcohol throughout the day and actively fight off thoughts or urges to drink might also be considered as having an alcohol-related problem, as well as being at risk to resume problem drinking. The behavior described above can be assessed quite easily by having subjects keep track of or recall the number of situations they purposefully avoided because alcohol was available, or by counting the number of alcohol-related thoughts or urges they had each day. Such data also can be used to study antecedents of a relapse to drinking.

As a central nervous system depressant, alcohol can have an acute effect on cognitive functioning. In fact, studies have shown (Fine and Steer 1979; Freund 1976) that many chronic alcoholics exhibit varying degrees of clinical and subclinical brain damage due to heavy excessive ethanol consumption. Given these results, it seems necessary to assess subjects' cognitive functioning and to evaluate posttreatment changes in neuropsychological functioning as it relates to drinking.

Finally, in addition to assessing alcohol consumption, all other drug use, prescribed and nonprescribed, should be measured. Such information is important for two reasons. First, alcohol is synergistic with many drugs, and its use may result in greater health dysfunction if it is used in conjunction with other drugs. Thus, it is essential to know if any concomitant drug use is occurring along with alcohol consumption. Dysfunction from other drugs can be evaluated only by asking about all types of drug use or abuse, both pre- and posttreatment. Second, when alcohol consumption is significantly reduced or eliminated, it is important to know whether other drug use or abuse is occurring.

Followup Interviews

A final set of issues concerns how frequently outcome data should be collected. Most alcohol treatment outcome data have been gathered during a single followup interview, conducted several months or years after treatment discharge. Two major problems have been identified with the single interview (Sobell 1978*a*, *b*). First, an extended interval from the time of treatment discharge to followup makes it difficult to locate and find all subjects in a study and, as mentioned earlier, high subject attrition can positively bias outcome conclusions.

The second problem with long followup intervals involves asking subjects to recall precise events and behaviors accurately. One solution to these problems is to collect outcome data more frequently during the followup period. The few studies that have used frequent followup interviews with alcohol abusers have located a remarkably high percentage of subjects for followup (Ersner-Hershfield et al. 1979; Sobell and Sobell 1976). Frequent followup contacts also allow for the collection of more precise outcome data, including daily reports of ethanol consumption as well as daily measures of other life-health variables such as number of days of missed work.

The opportunity for developing rapport with subjects and thereby encouraging more accurate reporting is more likely to occur when using multiple subject-interviewer contacts than when conducting a single followup interview. Frequent followup contacts also provide an opportunity to reconcile differences in data sources (a subject fails to report an alcohol-related arrest but a routine check of official police records indicates an arrest; a subject reports no drinking during a followup interval but the collateral's report indicates some drinking occurred). In such cases, at the next followup contact, the interviewer can ask the subject to explain the discrepancies. It might be expected that, regardless of whether the discrepancies are the result of subjects' deliberate deception or simple oversight, the subjects' subsequent reports might be more accurate because they know their responses will be checked. Thus, subjects who are initially deceptive in reporting might be led into providing more valid self-reports.

A final reason for using frequent versus single followup interviews is simply one of efficacy. The two major benefits of conducting frequent followups are the avoidance of subject attrition and the receipt of more sensitive and complete outcome data. However, more frequent interviews appear to take more time and planning. A comparative cost and time study of one-time versus frequent followup contacts has not been reported, but a recent study using monthly followup contacts with alcohol abusers has indicated that a fairly complete series of questions assessing multiple areas of life-health functioning, including daily drinking behavior, can be conducted by telephone and takes an average of 10 minutes per subject per month when averaged over 12 months (Ersner-Hershfield et al. 1979). Thus, monthly contacts might require more initial attention and planning, but the total amount of time and energy required might be equal to or less than that expended on a single followup interview, especially when one considers the time and resources spent tracking and locating lost subjects or the implications of drawing conclusions from a less than representative sample of all subjects in a study.

Summary

This paper discussed issues relating to the structure of alcohol treatment outcome evaluations, and new and more sophisticated procedures and methods for more precisely and accurately measuring the effectiveness of alcohol programs. Considering that only a decade ago many of these procedures were hardly within the realm of speculation, it is clear that the alcohol field has made remarkable advances.

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PATHS OUT OF ALCOHOLISM*

George E. Vaillant

Our understanding of alcoholism is enormously hampered by our needs—both for long-term followup studies of treatment and for adequate studies of the natural history of the disorder. All the existing prospective studies of the development of alcoholism are flawed by one or more of the following: high attrition, small sample size, followup only to age 30, and premorbid selection bias of antisocial children (Kammeier et al. 1973; McCord and McCord 1960; Jones 1968; Robins 1966).

This very preliminary report refers to two samples (from Harvard Medical School's Study of Adult Development) that attempt to rectify some of these needs. These two samples are briefly shown in table 1. One hundred and eighty-eight college students (the college sample) were selected for a health study in their sophomore years and have been followed every 2 years until age 55 (Vaillant 1977). The 456 inner-city men (the core city sample) were selected at age 14 in junior high school by Sheldon and Eleanor Glueck at Harvard Law School as a control group for their prospective study on juvenile delinquents (Glueck and Glueck 1950, 1958).

As can be seen in table 1, the two samples differed enormously in social class and educational opportunity. The core city men were reinterviewed by the Gluecks at ages 25 and 31; recently 400 of the original 456 men were restudied at age 47. When originally studied by the Gluecks, careful social service records were obtained on all of their families, making possible the prospective determination of ethnicity, alcoholic heredity, and childhood strengths and problems.

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* This work was supported by the W. T. Grant Foundation, Inc., and grant AA-01372 from the National Institute on Alcohol Abuse and Alcoholism.

Table 1. Comparison of Core City and College Samples

Sample Differences	Core City	College
Age when childhood assessment made	14±2	19±1
Year of birth	1929±2	1921±1
Number in original sample	456	204
Percent with parents who attended high school	33	94
Percent with parents in Social Class* IV or V	89	4
Percent with parents in Social Class* I or II	1	80
Average score on childhood strengths scale (Vaillant 1977)	9.2±5	9.5±5
Average IQ	95±12	c125-140
Percent of subjects who graduated from high school	48	100
Percent of subjects who attended graduate school	2	76
Percent in social class* I or II at age 47	9	98
Percent in social class* IV or V at age 47	49	0
Percent in health-sickness rating scale (HSRS)<70 (Luborsky, 1962)	28	20

*Hollingshead Two-factor Index of Social Class (Hollingshead and Radlich 1958)

As shown in table 2, attrition has been quite small. All 456 junior high school students have been accounted for. Either documented evidence of death or positive evidence of survival and geographic location at age 45 has been obtained. Less than 10 percent have either withdrawn from the study or provided data that are inadequate to make a reasonable judgment about their use or abuse of alcohol.

Table 2. Attrition in the Core City and College Samples

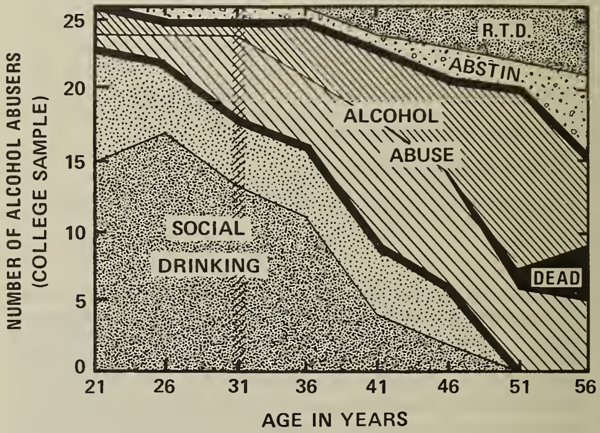
Sample Status	Core City	College
Number in original sample	456	204
Lost	0	0
Died prior to reinterview at 47	30	10
Withdrew from stduy but still alive	19	6
Data set incomplete but still alive	15	0
Data set virtually complete (At age 47)	392	188

Of 400 core city men for whom drinking histories from age 20 to 47 were obtained, 110 presented four or more symptoms of problem drinking. These symptoms were from a 16-item scale (Vaillant 1979), which gave one or two points (depending on the severity) if the individual had alcohol-related problems in each of four areas: work, social relationships, the law, or health. The scale allotted one to three points for varying amounts of treatment received for alcoholism; and one to five points based on the common symptoms of alcoholism (blackouts, admission of "loss of control" of drinking, morning drinking).

Seventy-one (18 percent) of the 400 men met the criteria for alcohol dependence established in the third revision of the *Diagnostic and Statistical Manual (DSM III)* and 70 men manifested seven or more problems on the Cahalan problem drinking scale (Cahalan 1970). There was also a 75 percent overlap among individuals identified by *DSM II* and *DSM III*.

In contrast, only 26 of 188 college men had multiple problems with alcohol, and only 5 percent met the *DSM III* criteria for alcohol dependence. Figure 1 presents a composite picture of the course of alcoholism in the 26 college graduates with problem drinking. At age 30, almost none had lost control of their use of alcohol. By age 55, a significant number had emerged from problem drinking to abstinence or social drinking. (Social drinking was defined as drinking more frequently than once a month, but having had no alcohol-related problems for a year or more.)

Figure 1. Followup of College Sample from Age 21 to 56



A composite graph showing the proportion of 26 college graduates who presented multiple symptoms of problem drinking at any given age. The light stippling indicates men who were heavy social drinkers; the more widely spread diagonal lines represent men whose alcohol abuse was modest or uncertain. R.T.D. the men returned to social drinking.

The composite life summaries of the problem drinkers in the core city sample reveal a very different pattern. By age 31, more than half of the 110 core city men who later became problem drinkers had lost control of their drinking. In part, this earlier onset was because 25 men from the core city sample and only one from the college sample manifested sociopathic traits (as defined by Robins 1966). By age 47, more than half of the core city problem drinkers had become abstainers or social drinkers. In both the core city and the college samples, death from alcohol-related illnesses did not become important until after age 40.

Table 3 defines what is meant by abstinence. Of the 400 men for whom complete data were available, 110 could be defined as problem drinkers. Of these, 49 were abstinent for 1 year or more. Thirty-nine of the 49 abstinent men were among the subsample of 71 who were not only problem drinkers but alcohol dependent according to *DSM III* criteria. Only 9 of the 18 men who resumed social drinking could be described as alcohol dependent; more surprising, only half of the men who were still active problem drinkers could be defined as dependent. In other words, being alcohol dependent or having many alcohol problems appeared to facilitate abstinence. Both the individual who only drives his wife to distraction with his drinking and the individual who has been stopped for drunken driving for the first time may be excellent candidates for a return to social (or at least to controlled) drinking if they are without other problems. In contrast, the individual who in the past has been detoxified; and who has past evidence of multiple problems with the law, his health, and his family; and who has made prior treatment attempts, is a very poor candidate for a return to social drinking.

Eleven of the 49 abstinent men (table 3) were abstinent for at least 1 year, and then relapsed to chronic drinking. This finding contradicts shorter followup studies, which claim that if an alcoholic is abstinent for 6 months, remission can be considered stable (Armor et al. 1978). Of the 49 abstinent men, 16 were abstinent for less than 3 years, but were still abstinent at the most recent followup. The third group of 21 men consisted of those alcoholics who had achieved 3 years or more of stable community abstinence. What was particularly noteworthy about these three groups was that no premorbid factors differentiated them from each other or from the still-active alcoholics.

If premorbid personality is unimportant, the next important question is: What leads to abstinence? What, indeed, are the paths out of alcoholism? The answer is neither "burning out," "hitting bottom," nor "spontaneous remission." Recovery from alcoholism is also not usually due to clinic treatment per se. The treatment experience of the 49 core city men who achieved at least 1 year of abstinence reveals that specific treatment seemed relatively unimportant during the year they became abstinent. Only 8 percent of the men received psychotherapy, only 8 percent received disulfiram, and 6 percent experienced help from a halfway house. Indeed, only 30 percent of the men who achieved a year of abstinence received any professional treatment. For men who achieved a year of abstinence, "self-treatment" appeared to be more useful (table 4). Alcoholics Anonymous helped 37 percent, and 49 percent felt that "will power" was important. As discussed later, many nonspecific therapeutic factors underlie "will power."

Table 3. Outcome of the 110 Alcohol Abusers in the Core City Sample

1.	Total number of adequately studied alcohol abusers		110 men
	Never abstinent for a year (38 active alcoholics, 18 men who returned to controlled or "social" drinking and 5 dead)		-61 men
2.	Ever abstinent:		49 men
	Of these	(a) Relapse to intermittent alcohol abuse	-5 men
		(b) Relapse to "progressive" alcohol dependence	-6 men
3.	Currently abstinent (for at least 1 year):		38 men
	Of these	(a) Abstinent for 4 years in nursing home	-1 man
		(b) Abstinent more than 3 years but binges more often than 1/year or periods of social drinking	-3 man
		(c) Abstinent in community but for less than 3 years	-13 men
4.	Securely abstinent in community for more than 3 years (mean = 10 years)		21 men

The men in the college sample who abused alcohol possessed the education and the income to obtain psychotherapy; these 26 college problem drinkers received 5,000 hours of psychotherapy. Ten of them received more than 100 hours each. But of these 26, only 1 (or possibly 2) appeared to regain control of alcohol use or to achieve abstinence as a direct temporal consequence of psychotherapy.

Table 4. Percentage of Abstinent Men Experiencing Different Professional Treatments During First Year of Abstinence

Treatment Experience	Men Abstinent >1 Year N=49
Psychotherapy	8%
Antabuse	4%
Halfway House	6%
Alcohol Clinic/Hospital	30%
Alcohlics Anonymous	37%
Only "Will Power"	49%

The disappointing results of treatment observed in these two longitudinally studied community populations are similar to those observed in clinical populations. Table 5 suggests that in comparable populations the results of detoxification and counseling (Bruun 1963; Robson 1965; Belasco 1971; Van Dijk and Van Dijk 1973) are not dramatically more effective than those reported for samples of alcoholics who applied for clinic admission but received little or no treatment (Kendall 1966; Orford and Edwards 1977; Imber et al. 1976).

What, then, are the paths out of alcoholism? Table 6 shows the frequency of the appearance of several nonspecific therapeutic experiences in the lives of the core city men who achieved abstinence. These factors are easily obscured by the facile explanation "will power." First, half of the men who achieved a year or more of abstinence found a substitute for drinking. For 5, it was meditation; for 7, chainsmoking; for 9, compulsive hobbies; for 10, candy, Valium, or Librium. And the men also discovered numerous other less common substitutes. Second, although none of the core city men received behavior modification therapy as a result of deliberate clinical treatment, about half of the men experienced some kind of "naturalistic" behavior modification or source of external control. For two men, this control was disulfiram. One of the problems of disulfiram treatment, however, is that it takes alcohol away without providing a substitute. For many patients, this behavior modification was mediated by disturbing medical complaints (ulcer, insomnia) that compelled them to be conscious of any excess drinking. For some men, the behavior modification was through compulsory supervision. A third factor associated with remission in more than half of the men was the discovery of a stable source of increased hope and self-esteem. For 12 percent, this source was increased religious involvement, and for 37 percent it was involvement in Alcoholics Anonymous (AA). Such involvement

Table 5. Comparison of Selected 2-Year Followup Studies

Followup Status	3 pooled "no treatment" studies[a]	Four "treatment" studies[a]
	n followed/ original sample 214/245	n followed/ original sample 685/963
	2-3 years	2 years
Abstinent or social drinking	17%	21%
Improved	15%	16%
Dead or Unimproved	68%	63%

[a] These are the studies by Orford and Edwards (1977), Kendall and Staton (1966) and Imber et al (1976). Because at 1 year there was no difference between Orford and Edwards' treated and control population and because at 2 years, their report did not clearly separate the two populations, all 85 of their subjects on whom they had 2 year follow-up are included.

[b] These are the studies by Belasco (1971), Bruun (1963), Robson (1965) and Van Dijk and Van Dijk (1973).

does not prove that AA caused the abstinence; in a naturalistically derived sample, such a high proportion of men using AA suggests that, at least in Boston, AA may reach a greater number of the alcoholic population than do alcohol clinics. The fourth factor found in many of the lives of the men was a fresh, close human relationship, uncontaminated by the old resentments, injuries, and guilts that alcoholics inflict on those who care about them.

Table 6. Percentage of Abstinent Men With Different Nonprofessional But Therapeutically Useful Experiences During First Year of Abstinence

Nonprofessional Experiences		Ever Abstinent n=49
I.	Substitute Dependency	53%
II.	Behavior Modification	
	Compulsory supervision or sustained confrontation	24%
	Immediate medical consequences	49%
III.	Increased hope/self-esteem	
	Increased religious involvement	12%
	Alcoholics Anonymous	37%
IV.	Social rehabilitation	
	New love relationship	32%

If these four factors are considered as a group, it can be seen that many successful treatment programs have consciously or unconsciously incorporated one or more of them. Indeed, the efficacy of AA, which incorporates all four, may be analogous to the success of the old wives' remedy of foxglove leaves for congestive heart failure. Both treatments wittingly or unwittingly contain active therapeutic ingredients. AA provides a substitute for alcohol dependence, behavior modification against its additional use, fresh social relationships, and a spiritual antidote for demoralization and hopelessness.

The final question that must be asked of a study of the naturalistic paths out of alcoholism is: If a problem drinker becomes stably abstinent, so what? Is an alcoholic who is not drinking really any better off than an alcoholic who continues to drink? Certainly the oft-quoted study by Gerard and Saenger (1966) suggests that social rehabilitation may be far more important than facilitating abstinence. In 50 abstinent alcoholics from a clinic population (Gerard and Saenger found that, after 3 to 5 years, more than half were still seriously disabled emotionally. Understandably, they wondered how much abstinence had really accomplished. In the present study of a nonclinic population, the results of abstinence are more encouraging. Excluding men who returned to social drinking or who had only a few alcohol-related problems, the outcome can be divided into four heuristically useful categories. First, the 227 core city junior high school youths who, by age 47, had never experienced multiple drinking problems; second, the 21 men who had been abstinent for more than 3 years; third, the 29 who, at age 47, were active alcoholics; and fourth, the 16 former alcoholics who had been abstinent for less than 3 years. The four groups could not be premorbidly differentiated in terms of childhood factors known to affect adult mental health. However, the current mental health as measured by Luborsky's (1962) Health Sickness Rating Scale was severely impaired among the active alcoholics and also among the recently abstinent alcoholics. In contrast, the mental health of men who had achieved stable abstinence resembled that of the men who had never become alcoholic. The implication, then, is that the longer an individual is abstinent, the less he will resemble the "personality disordered" alcoholic, and the more he will resemble the individual with lifelong sobriety. The converse also seems to be true. Alcoholics become anxious and depressed because they have lost control of their alcohol consumption more often than the anxious and the depressed become alcoholics. This situation may be analogous to that of prisoners of war released from North Vietnamese and Korean prison camps. Despite being theoretically "cured," for their first 2 or 3 years of freedom, they experienced a high rate of depression, suicide, and occupational and marital instability. However, after enough years had passed to heal the wounds, POWs tended to resume normal lives.

The overall intent of this paper is to suggest that there may be discrepancies between the true natural history of alcoholism and preconceptions about that natural history. Preconceptions may be biased by the fact that usually only alcoholics who come to clinics are studied, and those patients are studied for too short a time. The syndrome of alcoholism may have a relatively good prognosis; the return to social drinking may be as common an outcome as resorting to stable abstinence; the goal of abstinence for severe alcoholics, however simplistic, appears to correlate with more global assessments of social rehabilitation; and the relative ineffectiveness of clinic treatment does not mean that rehabilitation is impossible. The success of the natural healing processes of Alcoholics Anonymous and of behavior modification therapy (Sobell and Sobell 1978) may lead to further improvements in therapeutic efficacy.

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THE EVALUATION OF THE ALCOHOLIC: GENERAL DISCUSSION

Jerome H. Jaffe

Each of the more than 20 papers presented at this conference merits a considered critical commentary, and it would be presumptuous to assume that such a task could be accomplished by any single discussant within the confines of a single paper. I assume, then, that if one discussant whose major interest has been drug dependence is asked to comment on all the papers at a conference on alcoholism, it is not because of any special variety of omniscience. Rather, what is desired is a response to the gestalt of the conference, viewed from the vantage point of an interested and sympathetic but relatively ignorant colleague.

Before I comment on the papers themselves, I would like to mention that, for me, this was an unusual meeting. Over the past decade I had come to expect large meetings on topics related to drug abuse to be occasions for political and philosophical debate, shedding more heat than light. It has been many years since I attended a conference so characterized by scientific and scholarly presentations directed at important issues that were relevant to both researchers and clinicians. Perhaps it is the special mix of participants, or the locale, or perhaps we are moving into less turbulent times. But, whatever the reason, a word of appreciation is due to the organizers and the sponsors and the participants.

One major motif ran through this conference, played in many variations and recurring again and again: there are large gaps that exist between our emerging appreciation of the complexity of the problem we call alcoholism and our current efforts to intervene and to evaluate the impact of our interventions.

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Quantification

This motif was first heard clearly and without embellishment in the papers by Dr. Pattison and Dr. Marlatt (the latter delivered by Dr. Thomas Babor). Both made it clear that when we examine the issue carefully serious doubt arises about our capacity to reliably define the very problem—alcoholism—that brought us together. Dr. Pattison told us that the National Council on Alcoholism (NCA) criteria yield both false negative and false positive diagnoses, that they are no better in this respect than a simple self-report paper and pencil test like the MAST, and that they do not yield any sort of differential diagnosis or an index of severity. Dr. Marlatt continued the assault on current definitions by questioning whether a "disease model" (in which the patient either does or does not have the disease) could ever be as adequate as a "social learning model," which permits various patterns of behaviors exhibited to varying degrees.

Dr. Shaw then described the status of current efforts to overcome the unreliability of patient self-reports about alcohol intake by measuring alcohol-induced biological changes such as the plasma levels of α-amino-n-butyric acid (which is increased by chronic alcohol ingestion and which remains elevated for several days after alcohol cessation). We were told that after appropriate corrections are made for the effects of dietary protein deficiency by factoring in the levels of leucine, and taking into consideration the levels of the enzyme gamma glutomyl transpeptidase (GGTP), a diagnosis of alcoholism made from plasma levels will be correct 80 percent of the time, with only 1 percent false negatives, when patients with severe hepatic decompensation are excluded. The test was said to have potential value for monitoring relapse. Unfortunately, the high level of daily alcohol use required to produce these changes in humans made many listeners feel that we were far from the time when we could dispense with interviews, paper and pencil tests, and clinical sensitivity.

Alcoholism and Psychopathology

The theme of the inadequacy of our conceptual model (alcoholism is a disease that one either has or does not have) was repeated with new variations by Drs. Cadoret and Costello. Dr. Cadoret reminded us how often alcoholism is associated with other diagnosable psychopathological conditions, such as depression and sociopathy—conditions that frequently antedate the alcoholism itself and in large measure influence its clinical course. Furthermore, alcoholics with sociopathy (at least those seen in treatment) are more often depressed and are more likely to have attempted suicide. Dr. Costello made a convincing case that while the current dichotomous disease model is unsatisfactory, we should not look for any quick and simple resolutions from a factor analysis approach to the alcoholic personality.

Just as we began to wonder how we could continue to render clinical service in the face of such gross inadequacies in our capacity to diagnose and to properly categorize those who seek our help, Dr. Lee Robins described, with her characteristic blend of scholarship and pragmatism, the current status of the *DSM III* criteria for alcoholism and alcohol abuse. *DSM III*, which for better or worse will be with us for the next decade, is now a multiaxial system. Unlike its predecessor, *DSM II*, it permits us to specify on axis I additional diagnoses, and on additional axes personality types, degree of social stress contributing to the present illness, and highest level of functioning prior to the present episode. Furthermore, making a distinction between alcohol abuse and alcohol dependence, *DSM III* introduces a semiquantitative notion of severity. While a *DSM III* diagnosis is still far from a quantitative multifactorial description of a syndrome, neither is it a simple labeling. Dr. Robins reminded us that even science must strike bargains. In this case our new criteria for diagnosis of alcohol-related problems represent a compromise that permits us to continue to work even while we seek better criteria for subtypes that are closer to the findings of population heterogeneity that are now emerging.

Alcoholic Pedigree, Sex Differences, and Risk

In the next papers, Drs. Goodwin, Hesselbrock, Reich, and Tarter considered the genetic and biological contributions to what appears to be a vulnerability to developing alcohol dependence. Dr. Goodwin recognized the inadequacies in many studies of inheritance, but still concludes that the evidence is overwhelmingly persuasive that some people, biologically, are at greater risk for developing alcohol dependence. The risk for this syndrome appears to be relatively specific. Women are less likely to exhibit the syndrome than men and are more likely to report psychological problems or depression antedating the onset of the syndrome. Dr. Reich informed us that genetic vulnerability interacts with the environment, that alcoholics do not mate randomly, and that the presence of other syndromes such as antisocial personality increases the likelihood of heavy drinking. Dr. Tarter extended this line of inquiry by describing how a history of childhood hyperactivity (MBD) is associated with an increased severity of alcoholism. Each of these excellent papers shared one common conclusion—that a diagnosis of alcoholism without some consideration of subtype and recognition of different contributory biological factors is clearly inadequate for research purposes and is probably inadequate for the development of effective interventions.

Behavioral Assessment of the Alcoholic

The next papers, by Drs. Ludwig, Mello, and Nathan, considered the various ways in which environmental factors, learning, conditioning, and schedules of reinforcement contribute to the initiation and maintenance of alcohol use and to relapse after a period of abstinence.

Dr. Ludwig's description of his work on conditioned craving and loss of control was accompanied by an eloquent plea to avoid the false sense of security that occurs when we find fatal flaws in either extreme environmentalist or biological viewpoints. Both extreme positions, according to Ludwig, are straw men: demonstrating the inadequacy of an extreme biological view does not demonstrate the adequacy of an environmentalist position. The reverse is equally true. Both positions have validity and are necessary to a complete understanding of alcohol-related behavior.

Dr. Mello challenged the comfortable view that we drink because it makes us feel good. In laboratory studies chronic alcohol use often produces unpleasant effects; furthermore, even initial use is sometimes dysphoric. Perhaps, she argued, we should abandon the notion of drug-produced pleasure and pain in trying to understand drug use and focus on the behavior. Recent work shows that animals will self-administer electric shock and that opiate-dependent monkeys will self-administer naloxone. Alcohol use may represent, at least in some cases, stimulus self-administration. Events that maintain behavior should be considered reinforcers: we need not assume they are associated with "pleasure" and we are often wrong when we do.

Dr. Nathan described his work on laboratory analysis of drinking behavior, emphasizing that even among alcoholics (who are presumed to have craving and loss of control), environmental conditions (social interaction, anxiety, stress, the behavior of drinking companions) have a profound effect on drinking behavior.

These three papers are in essential agreement in underscoring the importance of the environmental variables in influencing drinking behavior. Some members of the audience were left wondering, however, about how this perspective could accommodate the existence of antecedent disphoric states. Nevertheless, the net impact was to further emphasize the kinds of information that are rarely if ever recorded in clinical programs (e.g., the psychological and physiological responses to alcohol itself; the accentuation of craving by alcohol-related stimuli), and the additional dimensions along which individuals with alcoholism might differ.

Negative Outcome and Relative Versus Absolute Risk

The interesting and scholarly papers by Drs. Scheig, Lieber, and Eckardt reminded us that alcohol may be one of the more toxic materials in the human environment and that when used in high doses it wreaks havoc with virtually every organ system studied. The high prevalence of impaired central nervous system (CNS) function among alcoholics (an impairment that may occur earlier than liver damage) has implications for treatment. It also underscores the importance of knowing more about the quantitative aspects of this damage and the possibilities of recovery, especially in the light of findings that few alcoholics achieve long-term abstinence. As is the case with liver damage, it is becoming clearer that adequate nutritional vitamin intake does not necessarily prevent alcohol-induced CNS damage. Dr. Phillips indicated that the problem of precise quantification may be susceptible to a technological solution and described his "skin patch" for measuring alcohol in sweat.

Assessment of Treatment Impact

Last, we turned our attention to the problem of intervention, and we heard several viewpoints on our capacity to alter the natural history of problem drinking and alcohol dependence.

Dr. Armor reported on the second landmark study conducted by his group on behalf of NIAAA: a followup at 4 years of a sample of the patients originally surveyed at 18 months. He also clarified some of the points of misunderstanding about the first report, which found that at followup some former patients were not totally abstinent, but neither had they relapsed to an alcoholic pattern of problem drinking. What the first report did that, for some, was controversial was to define this pattern of drinking as a form of improvement, rather than a category of treatment failure or a stage in an inevitable progression toward relapse. As one who has worked with some difficult cases of drug dependence, I did not find this definition so controversial. Improvement is improvement, even if it is not "cure" and even if it is not permanent. Dr. Armor now concedes that it was a strategic error to label such drinking behavior as "normal drinking." I think he is right. I can imagine the reaction of people working with heroin users if improvement, i.e., noncompulsive use, were labeled "normal heroin use." However, the selection of the wrong terminology should not divert us from the main point. We need to recognize that outcomes are varied, and that there are several patterns of improvement; total abstinence is not the only valid criterion of improvement.

Unfortunately, one aspect of the controversy is not likely to die, because the same finding has appeared in the second study. Alcoholics over 40 who were heavily dependent and were abstinent at 18 months are more likely to be found in a state of remission than if they were drinking (even without problems). But younger alcoholics with low levels of dependence were more likely to be found free of problem drinking at 4 years if at first followup they had not been entirely abstinent.

Dr. Sobell's paper touched on the critical relationship between outcome criteria and the assessment of treatment efficacy. Among the problems noted were those of definitions of validity, reliability, and quantification, of gaining support of programs to collect data, and of frequency of collection. The case was made that different patients may exhibit different patterns of response along each of the several dimensions that reasonable people might accept as indicating improvement. The changes on these dimensions may occur at different rates, necessitating observations at more than one point in time.

Dr. Skinner's paper on the problem of developing specific kinds of treatment for different patients with alcoholism reviewed the methodological obstacles to demonstrating that matching patients to specific interventions is either effective or worth the effort. According to Dr. Skinner, the major obstacle is probably not the availability of instruments and techniques for subdividing the populations; there are a number of ways (e.g., cluster analyses) that result in replicable subgroups of alcoholics. The problem may be that programs are often limited in the approaches used because they cannot function if too much philosophical diversity exists within the staff. Consequently, most patients get similar treatment and the effect of self-selection of different programs by varying kinds of patients tends to make demonstration of differential efficacy difficult.

In contrast to the other studies that began with patients first seen in treatment, Dr. Vaillant started with two populations not selected or self-selected because of alcohol problems; this permitted him to examine the "natural history" of alcohol problems, which he tells us cannot be accurately established from clinic populations. The paths into abstinence from the perspective of a whole population are very different than those seen from the perspective of the clinic.

Vaillant found that the majority of recoveries from severe alcoholism occur outside the framework of professional help. Griffith Edwards and his colleagues obtained a similar finding in their classic study of "treatment and advice." Lee Robins' followup of Viet Nam heroin users also noted that recovery had little to do with formal treatment. Vaillant reported that in Boston, Alcoholics Anonymous reached and helped more alcoholics to "secure abstinence" than did clinics, and warns us that the term "spontaneous recovery" is misleading. Like Peter Nathan, Arnold Ludwig, and Nancy Mello, Vaillant made the point that specific environmental events play important roles in the maintenance of alcohol-using behavior, and that it is the task of research to identify these events so they can be utilized for the benefit of those with alcohol problems. The importance of this search is underscored also by another finding. Vaillant's "core city" sample is not large—only 110 male alcohol abusers had adequate histories. But in that sample he found that more than half had never met his criterion of abstinence for a year and that only 21 achieved "secure abstinence." He tried to find some characteristics, either in their backgrounds or in the kinds of help they received, that would separate the successes from those less successful. Despite his perspective, Vaillant too tried to identify *types*, as did Armor, Skinner, and Sobell.

There is no way to do justice to or to summarize briefly Vaillant's important study, but I do want to point out that he too finds it necessary to use several measures of outcome that have quantitative dimensions. For example, abstinence is described as "never abstinent for a year"; "abstinent for a year" (used alcohol less often than once a month, and during the year not more than one episode of intoxication occurred and that of less than a week in duration); "currently abstinent" (which is further into secure abstinence—3 years, and less than 3 years).

Armor and Vaillant agree on at least one point—that for people who seek treatment the probability of "permanent cure" after a single treatment is exceedingly low (7 percent at 4 years in the Rand study). Armor and Vaillant also appear to agree that it is important to ask what factors are associated with these varied outcomes. Armor finds a number of strong correlations and interactions with age and marital status and the drinking pattern.

Although Dr. Vaillant can support the goal of abstinence for the alcoholics he has studied, he recognizes that even abstinence as it occurs in real life requires us to develop a more complex and quantitative concept. As he puts it, "Is 50 weeks' abstinence per year abstinence?" All of the participants at the conference agreed that outcome is more complex than the simple dichotomy of abstinent or relapsed.

In summary, the last set of papers on treatment presented another variation on the basic motif: Given a multidimensional problem, a heterogeneous population, and the possibility of change over time (with or without treatment) on several relatively independent dimensions, we need a multidimensional definition of improvement measured at several points in time.

Overall Review and Look at the Future

What impact will the findings presented at this conference have on research, on theory, and on treatment? I would feel more comfortable speculating on these questions if there had been some dissenting viewpoints. The areas of agreement were so wide that I am just a little suspicious that the data were preselected.

Considering the critical role of syndrome definition in research, there is little question that we will continue to see more work directed at achieving sharper definitions of the behaviors that concern us. The distinction between "subtypes" and a "quantitative multidimensional syndrome" is one that requires further conceptual effort. Should we strive to have our definitions consistent with the other psychopathological syndromes described in *DSM III*? If so, we should recognize that many environmental factors strongly influence the course of such syndromes as schizophrenia and affective disorder but are not necessarily viewed as dimensions of the disorder or as factors in creating subtypes. Despite the high genetic loading present in both of these disorders, *DSM III* has not yet proposed familial versus nonfamilial affective disorder or schizophrenia as useful subdivisions. It is likely, however, that some index of severity of the core pathology will be introduced. To do this for depression, the venerable term "melancholia" was resurrected. Is it time to look again at the term "inebriate"?

Workers in other areas have similar problems. In a recent multicenter study the proportion of patients who were diagnosed as schizophrenic was highly dependent on which set of diagnostic criteria was used (Overall and Hollister 1979). According to Samuel Guze, diagnostic (or classification) schemes imply the ability to predict. A useful classification is one in which each diagnostic group proves to be homogeneous: i.e., the cases in a given group demonstrate a uniform clinical picture and course, a predictable response to treatment, and a common etiology and pathogenesis. A classification scheme is not an end in itself; it is a tool, to be judged by how helpful it is in accomplishing certain purposes (Guze 1980).

Another area sure to receive continued attention is the notion of biological vulnerability. If, as current research indicates, a genetic factor not readily influenced by environmental factors during childhood contributes to the likelihood of developing alcoholism, numerous important implications exist, especially in connection with efforts aimed at prevention. Traditionally, given a vulnerable population, psychiatry has emphasized intervention at the earliest stages of life. It is difficult to conceive of interventions more radical than adoption into another family soon after birth. Yet, several studies suggest that, for males at least, this does not markedly influence the subsequent course of events with respect to alcoholism (Bohman 1978; Goodwin 1979). A better understanding of the nature of the seemingly specific vulnerability (or vulnerabilities) to developing alcoholism is an important step in any rational approach to prevention.

A related issue of great interest because of its importance to both research and theory is the relationship between conduct disorders and hyperactivity (minimal brain dysfunction, attentional deficit disorder) and severe alcoholism. Since our concepts and definitions for each of these syndromes are still evolving, there is clearly a need for additional work. Do such disorders affect the likelihood of alcohol problems or merely their severity? Given the paucity of whole population surveys studied over time and in enough detail to make these various diagnoses with precision, we are often limited to examining those patients who come to treatment. Since severity influences the likelihood of seeking treatment, it often is difficult to tease severity and likelihood apart. Even framing the question requires us to try to agree on a definition of alcoholism.

It would be of some interest to compare the characteristics of subjects with conduct disorder/hyperactivity who do not develop alcohol problems with those who do. Do the same adult environmental factors (stable marriage, satisfying job) that seem to be beneficial in the later adjustment of treated alcoholics (Bromet and Moos 1977) also protect against the development of alcoholism in high-risk groups?

We should also wonder if conduct disorders and hyperactivity are peculiar to Western industrialized societies. Would the relationship between these syndromes and alcoholism be as prominent in other societies where the role of the male is different or where alcohol use is far less common or entirely prohibited (as in some Moslem countries)?

The findings on alcohol-induced CNS impairment are bound to have substantial impact some day. When we recall the well-publicized outcries that have regularly followed the publications of CNS, endocrine, or immunological effects of illicit drugs like LSD or marijuana, the relative inattention given thus far to the repeatedly confirmed finding that alcohol produces CNS impairment in a substantial proportion of alcoholics is remarkable. Particularly startling are the recent findings by Lee et al. (1979) that more than half of young alcoholics under the age of 35 had evidence of intellectual impairment on either psychological testing or CAT scan, or both.

The obvious questions still not fully answered include: (1) Do subtle but measurable levels of CNS impairment accompany even social drinking (as several groups suggest) (Parker and Nobel 1980)? (2) Is the CNS in the younger drinker more vulnerable to such damage? (3) To what degree is alcohol-induced damage reversible? (4) Does reversal require total abstinence? These questions about CNS impairment are important for theory, policy, and prevention.

The answers may not discourage a confirmed alcoholic from continuing to drink any more than finding another adverse effect of tobacco deters the confirmed heavy smoker. But the answers may eventually lead to substantial changes in cultural attitudes toward alcohol use. Given the current view that the alcoholism rate increases as a function of average alcohol consumption level in a population (Royal College of Psychiatrists 1979), a decreasing acceptability of alcohol use could influence the incidence of alcoholism more than any conceivable new intervention directed at high-risk populations. Such a change should also force us to ask whether there are substances with functions similar to those of alcohol that are less toxic. Long-term comparative studies between alcohol and other substances with roughly similar actions would seem inevitable.

Last, we need to ponder the implications for treatment. In the United States, there is a remarkable similarity in content, techniques, and procedures used by a variety of programs specializing in the treatment of individuals with alcohol problems. Despite differences in setting (residential versus outpatient), these similarities persist even when the programs are sponsored by very different organizations, ranging from hospitals to religious groups. While some people do obtain "individualized" treatment from a few clinics, research-oriented programs, or private practitioners, it is more common to find that all individuals entering a given program obtain very similar treatment. Differences that do exist in the treatment received by different individuals are determined largely by the geographic, social, and economic factors that lead persons to enter one program rather than another. To a large extent, the personnel who operate many programs are paraprofessionals (often ex-alcoholics) or mental health professionals who share the beliefs of paraprofessionals about the importance of abstinence and self-help approaches. The notion that alcoholism is not an adequately descriptive term to determine the kind of treatment required will sound foreign to many of the workers, and it is difficult at present to envision the kinds of problems that may arise in trying to introduce the programmatic changes that logically flow from the research findings presented at this conference.

Several potential problems come immediately to mind. The first and most obvious is the need for an evaluation process as such. As long as the diagnosis of alcoholism is sufficient basis for deciding what interventions and what treatment methods are appropriate, and the only information required is that needed to determine whether an individual meets the established criteria for alcoholism, modest alterations in the criteria would have a relatively minor impact on the typical program. But if, as Drs. Pattison, Marlatt, Sobell, and Skinner imply, our definitions do not stand up to scrutiny and multifactorial and quantitative models (rather than all-or-none disease models) are needed to describe the kinds of people who seek help, then we need to ask what proportion of our treatment programs are currently making the needed assessments.

Perhaps psychiatric diagnosis, neuropsychological status, family history, and learned patterns of craving in response to alcohol and related stimuli all will be found to contribute significantly to the natural history of the problem and imply different kinds of intervention. What resources will then be required to make such a full assessment the standard rather than the exceptional practice that occurs only in research settings? And if these new assessments when introduced show incontrovertibly that there are indeed major subtypes, how will traditional programs respond? What of those individuals who have disabilities (depression, hyperactivity, sociopathy) that antedate their alcoholism, and that are not necessarily cured by abstinence alone? Should pharmacotherapy prove helpful in any of these conditions, what difficulties will arise in introducing such treatments into an atmosphere that is typically biased against "drugs" that affect behavior? Even more problematic is how treatment programs will respond to the emerging consensus that heavy drinkers may sustain significant brain damage even before their drug use affects such organs as the liver. If further research shows that ill effects are generally reversible with abstinence, the findings will fit in well with the major treatment goal of most programs and the other incentives generally put forth to motivate patients to strive toward that goal. And if further research shows that even "social drinkers" experience some adverse CNS consequences, those who now oppose, on theoretical grounds, behavioral approaches to controlled drinking may have a new and powerful argument.

We can only speculate about how such findings will affect the typical day-to-day operations of treatment programs. To what degree does impairment of memory or concept formation argue for therapies less dependent on cognitive skills? Can we realistically envision a segregation process within programs in which some patients are told that they are too impaired to benefit from a particular activity?

Another question raised by the emerging findings on alcohol-induced CNS impairment is what this will do to the image of the recovered alcoholic or industry-based intervention programs. Will it be as fashionable to publicly repeat the phrase, "I am an alcoholic," if that term comes to be synonymous with "high likelihood of impaired brain function"?

The findings of the latest Rand Corporation followup study that some individuals treated for alcoholism (and not just a tiny minority) can drink alcohol again without loss of control or rapid deterioration cannot be ignored. Other workers in the field have made similar observations (Edwards et al. 1977; Gottheil et al. 1979; Paredes et al. 1979).

Over the short term, the impact of these findings on the operations of the average treatment program are not likely to be profound. Programs will continue to advocate total abstinence for all patients, will continue to use disulfiram, and will continue to regard a resumption of drinking as a "slip." But the impact of such studies will be felt quickly by those charged with assessing the effectiveness of programs. It is now clear from the Rand study and others that improvement is not necessarily synonymous with continued abstinence. Further, abstinences can be associated with little or no improvement along interpersonal, vocational, and psychological dimensions, while improvement may occur in these areas in the presence of low to moderate levels of drinking. Thus, it is necessary to find reliable ways to measure behavior in these areas including quantitative measures of alcohol intake. We need not agree on which outcome measure ought to be given the greatest priority in order to agree that more than one measure is needed. Because these findings of noncorrelation between outcome measures are at odds with traditional beliefs, it will be important for future evaluation studies to pay careful attention to patient characteristics at intake. The capacity to drink again without eventual loss of control may be limited to certain subtypes.

Will the findings of subsequent nonpathological drinking in treated alcoholics eventually lead to more flexibility in setting goals for individual patients? Perhaps, but I am sufficiently impressed by the findings of CNS impairment that appear to show up even among social drinkers to speculate that the trend may well be in the opposite direction. If the findings hold up, and especially if subsequent studies show a dose relationship with no threshold effect, the Western investment in the intellect may lead even nonalcoholics to reduce their use of alcohol and may make abstinence fashionable behavior.

The studies showing that anxiety, depression, and poor functioning persist even during periods of abstinence should receive greater attention. Whether the kinds of depression and dysphoria that are experienced by even abstinent alcoholics (Pottenger et al. 1978) will respond to the treatments used for the major affective disorders is a question not yet answered in any systematic way. The interpretations of results of previous studies are open to question in light of recent findings on the importance of proper dosage and of controlling for plasma levels of the therapeutic agents used.

I cannot leave the subject of treatment without noting that our belief that treatment is of measurable value rests on a somewhat shaky foundation. Most studies that show effectiveness are based on comparing subjects who participate in treatment with those who drop out at intake. This hardly constitutes an appropriate control group. In one recent study, married alcoholics were randomly assigned to "treatment" (i.e., full services including in-patient detoxification if needed) or to "advice" with no further services after a single interview. No differences in outcome were found over a 1-year period of observation (Orford and Edwards 1977). This is not the first study to show no difference in outcome between intensive and less intensive interaction between treaters and patient. It simply carried the concept of minimum intervention as far as possible, consistent with the need to gather baseline and followup data and to treat all of those seeking help with compassion and dignity. There should be no need to emphasize the importance of additional studies with appropriate control groups in assessing the benefits of treatment.

For a decade or two, many in the field of alcoholism had a feeling that they knew what to do if only they had the resources. Over the past decade, there has been an unprecedented increase in available resources and treatment programs have expanded. Great comfort comes from knowing what to do when confronted with a problem. The careful, thoughtful research papers presented here, taken as a whole, should make us much *less* comfortable about what we know and how best to use our resources. Our discomfort is made more tolerable, however, by the realization that because resources for continued careful and thoughtful research have also expanded, our present uncertainties may be temporary.

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U.S. GOVERNMENT PRINTING OFFICE : 1981 O - 347-398

DHHS Publication No. (ADM) 81-1033
Printed 1981

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